

Novel mechanisms of innate immunity

Von der Fakultät für Lebenswissenschaften
der Technischen Universität Carolo-Wilhelmina

zu Braunschweig

zur Erlangung des Grades eines

Doktors der Naturwissenschaften

(Dr. rer. nat.)

genehmigte

D i s s e r t a t i o n

von Björn Bulitta
aus Wolfenbüttel

- 1. Referent: Professor Dr. Lothar Jänsch
- 2. Referentin: Professorin Dr. Dunja Bruder
- 3. Referent: Professor Dr. Stephan Dübel

eingereicht am: 3.8.2015

mündliche Prüfung (Disputation) am: 15.12.2015

Druckjahr 2016

Vorveröffentlichungen der Dissertation

Teilergebnisse aus dieser Arbeit wurden mit Genehmigung der Fakultät für Lebenswissenschaften, vertreten durch den Mentor der Arbeit, in folgenden Beiträgen vorab veröffentlicht:

Abschlussarbeiten

Bulitta, B. (2011). Modulation of NK cell effector function by kinase inhibitors, Masterarbeit, Technische Universität Braunschweig

Publikationen

Scheiter, M. & Bulitta, B., Van Ham, M., Klawonn, F., König, S., & Jänsch, L. (2013). Protein kinase inhibitors CK59 and CID755673 alter primary human NK cell effector functions. Front Immunol, 4(MAR).

Tagungsbeiträge

Bulitta B., Scheiter M., Garritsen H., Klawonn F., & Jänsch L.: Novel kinases involved in NK cell effector responses and microtubule dynamics. (Poster) 14th Meeting of the Society for Natural Immunity, Heidelberg (2013)

Bulitta B., Scheiter M., Gröbe L., & Jänsch L.: Proteomic definition of primary human MAIT cells. (Poster) 44th Annual Meeting of the German Society for Immunology, Bonn (2014)

Abstract

Over decades, one of the central dogmas of immunity has been that immune cells can be classified as parts of either the adaptive or innate immune system. In recent years, however, the lines between these two systems have become increasingly blurred. For example, subsets of innate natural killer (NK) cells have been demonstrated to display memory phenotypes, while recently identified mucosal-associated invariant CD8 T cells (MAIT cells) realize innate cytotoxicity. MAIT and NK cells both constitute predominant populations in human blood and other organs and share a high expression of CD161. NK cells detect virus infected, and abnormally transformed cells, and MAIT cells are able to identify and directly lyse bacterial-infected cells. While NK activation is controlled by a multitude of receptors, MAIT responses essentially depend on a TCR α chain that is invariant, as opposed to what is found in conventional T cells.

Although NK cell activation is well defined, the underlying signaling networks are still obscure. In the first part of this thesis, the role of several kinases in NK cell activity was investigated. It could be shown that chemical inhibition of CaMKII and PKD kinases, respectively, leads to a significant decrease of NK cell cytotoxicity and cytokine release, underscoring the importance of kinases CaMKII and PKDs in NK cell activation. Notably, these experiments also indicate significant donor-variations, inhibitory pathways and further involved cell types, which concertedly bias drug-modulated NK responses.

In the second part, new mechanisms of innate immunity were investigated for the first time in primary human MAIT cells. Currently, the exact role of MAIT cells in health and disease remains widely undefined, and proteomic data about this innate-like T cell subset is missing. Proteomes of primary human MAIT were quantitatively compared donor-dependently with innate NK cells and conventional CD8 T cells by mass spectrometry.

In total, 5500 proteins could be identified from five representative human donors. These data reveal a functional inventory of MAIT cells that integrates phenotypes from both NK and CD8 cells. Donor-dependent analyses then defined a MAIT-specific profile of effector molecules, and regulators of exocytosis and proliferation, respectively. Furthermore, this thesis provides candidates that can now be considered as novel MAIT markers and/or likely contribute to their anti-bacterial unique phenotype. In this context, the first observation of

the immunological synapse (IS) of a MAIT cell interacting with a bacterial infected target cell is presented and recruitment of candidate protein S100A4 to the site of anti-microbial activity is confirmed.

Contents

1	Introduction	1
1.1	Functions and components of innate and adaptive immunity	1
1.2	Function and activation of innate natural killer cells	4
1.3	The biology of adaptive cytotoxic T cells	6
1.3.1	Priming and activation of CD8 T cells	6
1.3.2	Formation of the cytotoxic T cell immunological synapse, and CD8 ⁺ T cell effector functions	9
1.4	Mucosal-associated invariant T cells	10
1.4.1	Phenotype of MAIT cells	10
1.4.2	Activation and function of MAIT cells	12
1.4.3	Development of MAIT cells	15
1.4.4	MAIT cells and diseases	16
1.5	Aim of thesis	18
2	Material and Methods	19
2.1	Equipment and software	19
2.1.1	Equipment	19
2.1.2	Software	19
2.2	Chemicals, buffers and media	20
2.2.1	Buffers	20
2.2.2	Media	21
2.2.3	Kinase inhibitors	22
2.3	Cells	22
2.4	Antibodies	22
2.5	Methods of Microbiology	24
2.5.1	Used bacterial strains	24
2.5.2	Cultivation and fixation of bacteria	24
2.6	Methods of Cell Biology	25
2.6.1	Culturing of cells	25

2.6.2	Isolation of PBMCs from human peripheral blood	25
2.6.3	Fluorescence activated cells sorting of primary human immune cells cells	25
2.6.4	Immunofluorescence analysis of MAIT cell activation	26
2.6.5	Flow cytometric analysis of MAIT cell activation	27
2.6.6	Magnetic activated sorting of human NK cells	27
2.6.7	NK cell degranulation assay	28
2.6.8	NK cell cytokine release assay	28
2.6.9	Flow cytometric analysis of NK cell degranulation and cytokine release	29
2.7	Semi-quantitative proteomic analysis	29
2.7.1	Cell lysis and digestion (urea lysis)	29
2.7.2	Reverse-phase peptide clean up and desalting	30
2.7.3	Peptide labeling with iTRAQ TM	30
2.7.4	Subfractionation of complex peptide samples through SCX chromatog- raphy	31
2.7.5	Mass spectrometric analyses and data interpretation	31
2.8	Statistical evaluation and determination of significantly regulated proteins . .	32
3	Results	35
3.1	The role of Src kinases, CamKII and PKD kinases in NK cell activation	35
3.1.1	Inhibition of Src kinases, CaMKII and PKD kinases decreases NK cell degranulation and cytokine release in primary human PBMCs	35
3.1.2	Donor-specific responses of pure NK cells treated with Dasatinib, CK59 and CID755673	37
3.2	MAIT cells isolated from human donor blood are suitable material for proteomic analyses	41
3.3	First insights into the proteome of primary human MAIT cells reveal T cell specific proteins and pathways	44
3.4	Mass spectrometry generates highly reproducible data from small cell numbers	52
3.5	Conserved and novel functions in innate immunity in MAIT cells	56
3.5.1	Flow cytometry allows the generation of highly pure MAIT cells, CD8 ⁺ T cell and NK cell samples	56
3.5.2	Protein identification in MAIT, NK and cCD8 ⁺ T cells shows large overlap of proteins in different donors	59
3.5.3	Differential protein expression in MAIT, NK and cCD8 ⁺ T cells	62

3.5.3.1	MAITs cells are a cell type distinct from NK and cCD8 ⁺ T cells on the proteomic level	62
3.5.3.2	Robust identification of regulated proteins in MAIT, NK and cCD8 ⁺ T cells indicates distinct proteomic profiles	67
3.5.3.3	Proteomic data is validated by flow cytometry	71
3.5.4	Immunological effector proteins show distinct abundance in MAIT cells	72
3.5.4.1	MAIT cells possess a unique set set of effector molecules . .	72
3.5.4.2	Proteins regulating exocytosis and proliferation are upregulated in MAIT cells	73
3.6	First-time characterization of the MAIT cell immunological synapse	77
3.6.1	Formation of the MAIT immunological synapses	77
3.6.2	S100A4 is associated with microtubules in MAIT cells	79
3.6.3	S100A4 localizes at the MAIT IS in a time-dependent manner	81
4	Discussion	87
4.1	Chemical inhibition of NK cell effector functions	87
4.1.1	Specificity of used kinase inhibitors	87
4.1.2	Role of PKD and CaMKII in NK cell activation	88
4.1.3	Perspectives for kinase inhibitors in cancer and NK cell therapy	89
4.2	Novel mechanisms of innate immunity in MAIT cells	91
4.2.1	Proteomic analysis of low-abundant primary immune cells	91
4.2.2	Proteomic results are in accordance with current knowledge	91
4.2.3	Is the definition of a “typical” MAIT cell possible with proteomics? . .	93
4.2.4	Best of both worlds: Typical MAIT cells between NK cells and CD8 T cells	94
4.2.5	Defining the typical MAIT cell phenotype with proteomics	95
4.2.5.1	A new set of markers for human MAIT cells	95
4.2.5.2	The arsenal of MAIT cells - innate immunity requires a specific pattern of effector molecules	96
4.2.5.3	Increased capacity for exocytosis in typical human MAIT cells	101
4.2.5.4	Controlling the killer: MAIT cells display a unique set of proteins that regulate proliferation	103
4.2.6	First insights into the molecular mechanisms of MAIT cytotoxicity . .	105
5	Summary and outlook	109
5.1	Coordination of NK effector function by kinases Fyn, CaMKII and PKD	109
5.2	Proteomic analysis reveals novel mechanisms of innate immunity in MAIT cells	110
5.3	First-time characterization of the MAIT cell immunological synapse	112

Appendix	115
List of Figures	179
List of Tables	181
List of Abbreviations	183
Bibliography	187
Acknowledgements	209

1 Introduction

1.1 Functions and components of innate and adaptive immunity

During the course of evolution, even the smallest of life forms have developed rudimentary protection mechanisms to shield themselves from the potential harmful influence of infectious agents. Larger and more complex organisms like *Homo sapiens* have to deal with a wide variety of pathogens that can rapidly evolve and adapt. Therefore, humans already possess several layers of defense that allow the human body to effectively prevent those pathogens from entering its system or, if this proves to be unsuccessful, fight the intruders with a variety of interwoven mechanisms.¹ The initial lines of defense are made up by physical or chemical barriers (Fig. 1), like the skin or antimicrobial proteins. When these barriers are breached, other components of the immune system get activated. Classically these mostly cellular-based components are divided into two subsystems, namely the innate and the adaptive immune response. While the innate immune response elicits a rapid, but unspecific response directed towards a broad range of pathogens, the adaptive immune system takes rather days than hours to establish protection. Even so, adaptive immunity is highly specific and able to eliminate infections even more efficiently. (Fig. 1) Importantly, cells of the adaptive immune response are also capable of exerting a memory phenotype, thereby preventing reinfection on a second exposure to the pathogen, and giving rise to long-lasting immunity.¹

Both subsystems of the immune response are mostly comprised of white blood cells or leukocytes (Fig. 2). The non-cellular complement system is part of the innate immunity and made of soluble factors.¹ Its components are able to quickly recognize and destroy foreign organisms. The cellular part of the innate immune response is made up of a variety of different cells of myeloid origin, namely macrophages, dendritic cells, mast cells and granulocytes. Macrophages are phagocytic cells and perform functions during innate and the adaptive immune response. They perform an important role during the first line of innate defense by phagocytosing invading microorganisms. Furthermore, macrophages coordinate immune responses by secreting cytokines and activating other immune cells. The name of granulocytes is derived from the typical densely staining granules, and their group is comprised of three cell

types: neutrophils, eosinophils and basophils. Neutrophils are also phagocytic and efficiently destroy taken-up microorganisms, while the less abundant eosinophils and basophils release cytotoxic and inflammatory granules upon activation. Mast cells are not well described, but have been shown to play a major role in allergic responses and the defense against parasitic worms. After macrophages and granulocytes, dendritic cells are the third type of phagocytic cells. They also degrade pathogens they have taken up, but more importantly are able to activate cells of the adaptive immune response by displaying antigens derived from the pathogen on their surface. Therefore, they are also called antigen-presenting cells (APC) and form a link between innate and adaptive immune responses. Natural killer cells (NK cells) are derived from a lymphoid progenitor, but are nevertheless considered a part of the innate immune response. The main function of NK cells is to efficiently detect and lyse abnormal cells, like virus-infected or tumor cells. Importantly, NK cells act rapidly and their activity is not controlled by receptors specific for certain antigens but rather a variety of germline-encoded activating and inhibitory receptors.

Cells of lymphatic origin, namely T and B cells, comprise the adaptive part of the immune response.¹ B cells bind to antigens through their B cell receptor (BCR), and afterwards differentiate into plasma cells. These plasma cells then produce specific antibodies, which are a secreted form of the BCR with identical specificity and therefore bind the same antigen. T cells are defined by the expression of the T cell receptor (TCR), and can differentiate into one of different effector cells. Helper T cells express CD4, and coordinate immune responses. They influence the function of B cells and macrophages. Regulatory T cells can restrain the activity of other lymphocytes and thereby dampen immune responses. Cytotoxic T cells show expression of CD8 and are able to efficiently kill infected cells that present the antigen specific for their TCR. During the course of an infection or antigen exposure, some B and T cells will develop into memory cells, that will rapidly become reactivated upon repeated exposure to the antigen, and by that provide long-lasting immunity.

Interestingly, recent observations have blurred the lines between innate and adaptive cell types. For example, NK cell subsets have emerged that show a memory phenotype, with enhanced activity of these already primed NK cells.^{2,3} Furthermore, T cell subsets like $\gamma\delta$ T cells or NKT cells have been shown to respond rapidly to more unspecific stimuli, displaying an innate-like phenotype.^{4,5} Most recently, the subset of mucosal-associated invariant T cells has been discovered. These so-called MAIT cells are highly abundant in mucosal tissues and the most abundant T cell subset in peripheral blood. They also display an innate-like phenotype and are able to detect and lyse bacterially-infected cells without prior activation.⁶⁻⁸

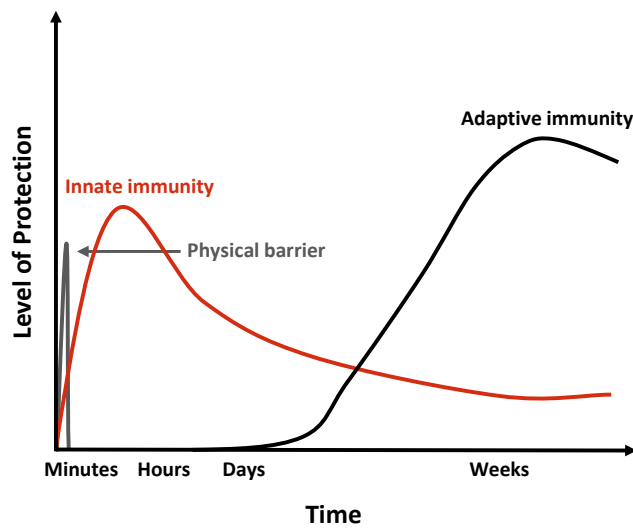


Figure 1 | The relation between the innate and the adaptive immune response. The first line of defense against pathogens are physical and chemical barriers, like the skin. Afterwards, pathogens have to face the quick but rather unspecific innate immune response, while the highly specific adaptive immunity gets active after some days (adapted from Kumar⁹).

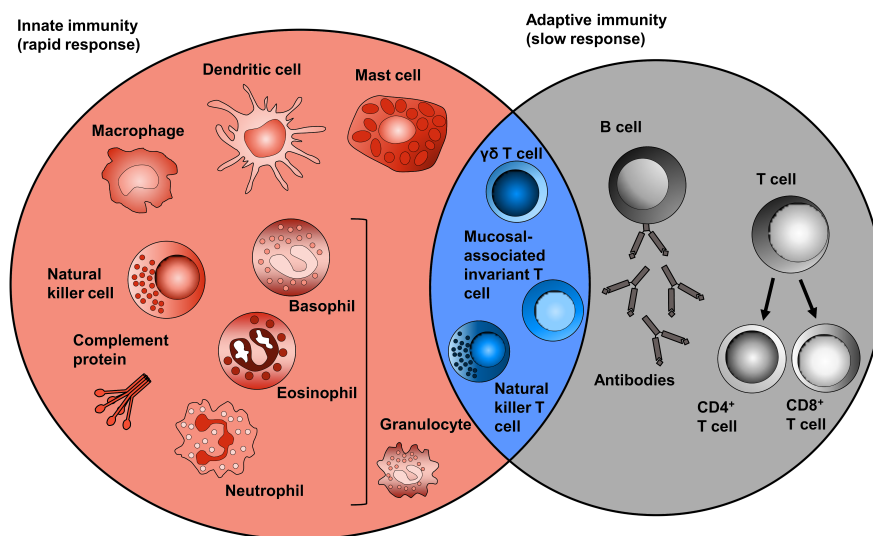


Figure 2 | Components of the innate and adaptive immune system. The immune system is classically divided into the innate and the adaptive immune response. While innate-immune cells like dendritic cells, mast cells and granulocytes are of myeloid origin, adaptive immune cells and NK cells are lymphocytes. Recently, lymphocytes like $\gamma\delta$ T cells, NKT, memory NK cells (not shown) and MAIT cells have been discovered, that display properties of both innate and adaptive immune cells (adapted from Dranoff¹⁰).

1.2 Function and activation of innate natural killer cells

Natural killer cells (NK cells) are cells that develop from a lymphoid progenitor and play a crucial role in the defense against viral infections and malignant tumors.¹¹⁻¹³ They aid the immune system through the effective killing of abnormal target cells by degranulating, as the cytolytic granules released during this process contain granzymes and perforin. The high cytotoxic potential of NK cells can also be directed against other immune cells, like dendritic cells (DCs), activated CD4⁺ T helper cells and hyperactivated macrophages (Fig. 3), thereby regulating the activity of the immune system.¹¹ Additionally, NK cells can enhance the capability of immune cells by the release of pro-inflammatory cytokines like tumor necrosis factor- α (TNF- α), interferon- γ (IFN- γ), thereby shaping the immune response by activating macrophages, dendritic cells (DCs) and T cells.^{11,14} Degranulation can be detected by the expression of lysosomal-associated membrane protein-1 (LAMP-1) on the cell surface. In CD nomenclature, LAMP-1 is known as CD107a, and a marker for cytolytic granules.¹⁵ During the process of degranulation, lytic granules fuse with the NK cell membrane and CD107a appears on the surface of activated NK cells.

In general, NK cells make up from 5 % to 20 % of the human lymphocyte population, and are defined as CD3-negative lymphocytes that express neural-cell adhesion molecule 1 (NCAM1), also known as CD56. Interestingly, NK cells can be classified into functionally distinct subsets by quantifying expression of CD56. The so-called CD56^{bright} cells express high amounts of CD56, make up approximately 10 % of all NK cells in peripheral blood and are usually associated with increased release of cytokines and lower cytotoxic potential.^{16,17} CD56^{dim} make up the majority of NK cells in peripheral human blood, show decreased expression of CD56 and are highly cytotoxic.^{18,19} Recent studies have revealed a new, CD56^{neg} NK subset that is very low abundant in healthy individuals but expands during chronic viral infections.²⁰ The exact role of these cells is still under debate.

In contrast to B and T cells, NK cell activity is not controlled by a variable, single receptor. NK cells rather express a variety of different, germ-line encoded receptors, enabling them to integrate inhibitory and activating signals that are expressed on target cells and detected by these receptors. The balance of signaling input then leads to a positive or negative response of NK cells to different stimuli.²¹⁻²⁷ NK cells can also mediate antibody-dependent cellular cytotoxicity (ADCC), which is mediated by activating Fc γ RIIIA receptor CD16.²⁸ This enables NK cells to detect and lyse cells that have been recognized by antibodies produced by B cells. Furthermore, NK cells can exert natural cytotoxicity independent of antigen recognition and leads to activation through the lack of inhibitory signals, that are usually mediated by the expression of MHC class I molecules.²⁹ This “missing self” activation mechanisms

render NK activation with immortalized K562 target cells extremely effective, as this cell line does not express MHC class I.³⁰ Additionally, K562 surface ligands also provide signals to activating NK cell receptors,³⁰ e.g. through ligands for NKG2D,³¹ NKp30³² and DNAM-1.³³ If an NK cell encounters a target cell displaying ligands for its activating receptors, the signal is mediated through the interaction with signaling adaptors (Fig. 4). A big proportion of activating receptors like CD16 or NKG2C are associated with adaptor proteins that contain immunoreceptor tyrosine-based activating motifs (ITAMs), for example CD3 ζ and Fc ϵ RI γ .^{34,35} However, adaptor proteins like DAP10 or SAP that bind to activating receptors NKG2D and 2B4, do not contain ITAM-motifs.²² NK cells also express a panel of inhibitory receptors, that can prevent them from killing cells presenting ligands to activating receptors. Most but not all of these inhibitory receptors recognize MHC class-I molecules.³⁶ Inhibitory receptors are associated with the presence of cytoplasmic immunoreceptor tyrosine-based inhibition motifs (ITIM), and their signaling can usually override activation signals and thus prevent killing of healthy cells.¹³ This activation and inhibition signals have their source at the contact interface between NK cell and target cell, the immunological synapse (IS).²⁷ Formation of the NK IS is a multiple-step process that has to be strictly controlled, and finally leads to the secretion of cytolytic granules and target cell death (Fig. 4). After establishing contact, adhesion molecules like LFA-1 mediate formation of tight junctions between NK and target cell, thereby already inducing intracellular signaling. Molecules like Src, LAT, ZAP70 and PKC kinases are phosphorylated,³⁷⁻³⁹ and additionally LFA-1 signaling triggers actin polymerization and granule polarization.^{40,41} At the contact site, molecules that mediate adhesion like LFA-1 segregate to the outer region of the synapse, the peripheral supramolecular activation cluster (pSMAC),⁴⁰ while activating receptors accumulate at the central SMAC (cSMAC). There, they trigger the relocation of signaling molecules like Src kinases, Vav1, ZAP70 and PKC kinases, as well as scaffolding proteins towards the synapse.²⁷ Also, the microtubule organizing center (MTOC) with the granules associated to it moves towards the IS, where they finally can be released.^{40,42}

Although the NK IS and NK cell activation have already been analyzed to a larger extent, these studies have focused on the components directly at the IS. Systematic studies of the signaling network that is induced was then carried out in a recent study by König and colleagues.⁴³ The authors described the kinase phosphorylation response that follows specific receptor stimulation of either CD16 stimulation, or synergistic stimulation of 2B4 and DNAM-1. Mass spectrometric analysis of phosphorylated kinase peptides revealed known and novel signaling components to be phosphorylated quickly after NK cell activation. In total, a network of 188 modified kinases was identified by mass spectrometry, and reproducible phosphorylation of SFK member FYN, Calcium/calmodulin-dependent kinase II (CaMKII)

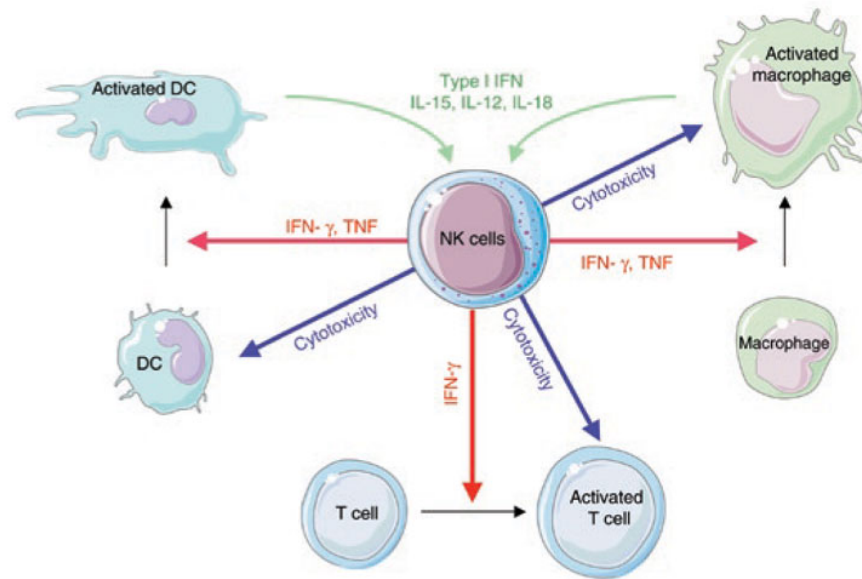


Figure 3 | NK cells adjust immune cell responses. NK cells can promote the immune response by triggering the release of inflammatory cytokines (red arrows). Additionally, they are also able to exert regulatory functions and kill activated T cells and macrophages, or immature dendritic cells (adapted from Vivier *et al.*¹¹).

and protein kinase D2 (PKD2) could be observed after receptor engagement.⁴³ However, data that show if these kinases actually play a role during NK cell activation are missing until now.

1.3 The biology of adaptive cytotoxic T cells

1.3.1 Priming and activation of CD8 T cells

As natural killer cells, CD8 T cells are of lymphoid origin. Their mode of action, however, is completely different. Unlike NK cells, CD8 T cells are part of the adaptive immune response, and therefore their activation is regulated differently. While NK cell activity depends on a variety of germ-line encoded receptors, T cells rely on the T-cell receptor (TCR). The TCR is expressed on every T cell, and made up from highly variant segments. Basically, every T cell receptor consists of an α and a β chain, and is therefore a heterodimer. Notably, a small subset of T cells expresses a T cell receptor that is made of $\gamma\delta$ chains. Nevertheless, both chains of the T-cell receptor are built from an amino-terminal variable region, a constant region, and a short stalk segment that connects both chains via a disulfide bond. Also, both chains contain a transmembrane domain with which they are anchored in the plasma membrane. In different T cell clones, the variable region is randomly combined from V and J segments in

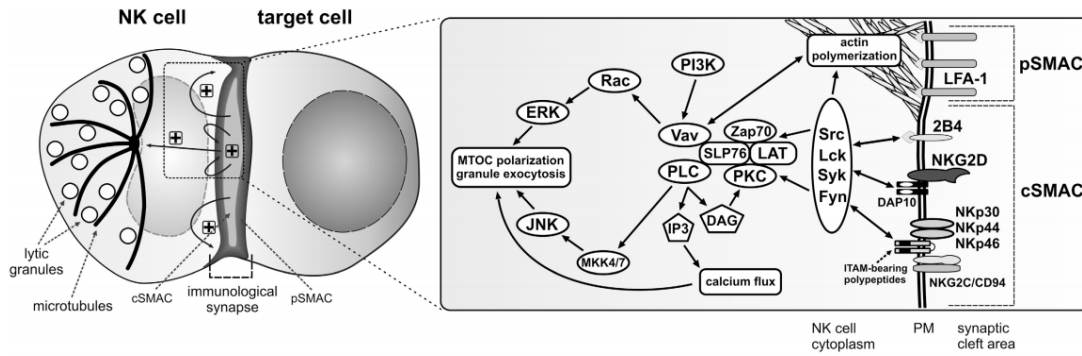


Figure 4 | Formation of the immunological synapse in NK cells. When an NK cell encounters a target cell that presents ligands to its activating receptors, an interface is formed that is called immunological synapse (IS). Molecules that mediate adhesion relocate to the peripheral parts of the synapse (pSMAC), while the activating receptors aggregate at the central part (cSMAC). Linking of these receptors with their ligands on the target cell results in signaling cascades, that are induced by phosphorylation of various signaling molecules. This promotes in actin polymerization at the pSMAC, and convergence of the microtubule organizing center (MTOC) and lytic granules towards the synapse. Afterwards, the granules are released towards the target cell and their contents induce target cell death by various mechanisms (adapted from Krzewski and Coligan²⁷).

the α chain, and from V, D and J segments in the β chain. This gives rise to a huge diversity of T cells with different TCRs, with each one specific for a different antigen. Importantly, the antigens need to be presented by major histocompatibility complex (MHC) proteins to be recognized by T cells. While MHC class I molecules are expressed ubiquitously, MHC class II molecules are specific for antigen presenting cells (APCs).¹

Usually, mature CD8 T cells circulate in the peripheral blood and lymphoid tissues, and are known as naïve T cells if they have not encountered their specific antigen. They continuously sample the peptide:MHC complexes that are presented to them by dendritic cells. The interaction between the cell types is mediated by lymphocyte function-associated antigen 1 (LFA-1) and CD2 on the T cell and intercellular adhesion molecule 1 (ICAM-1), ICAM-2 and CD58 on the dendritic cell. During this binding step, naïve CD8 T cells efficiently sample large numbers of MHC class II molecules on the dendritic cell surface. In case of a successful binding between TCR and peptide:MHC complex, signaling steps induce a conformational change in LFA-1 that leads to an increase of its affinity to ICAM-1 and ICAM-2. This leads to an even more stable interaction between T cell and APC.^{44–46} However, the signal transmitted by the interaction of TCR and peptide:MHC complex is not sufficient to fully activate the T cell on its own, and stimulate its proliferation and differentiation. The additionally required signals are also provided by the APC (Fig. 5A). The best-characterized co-stimulatory signal is delivered by the interaction of CD28 on the T cell surface and its ligand, B7 molecules, which results in optimal clonal expansion of T cells.^{47–49} Also, CD28 ligation increases the

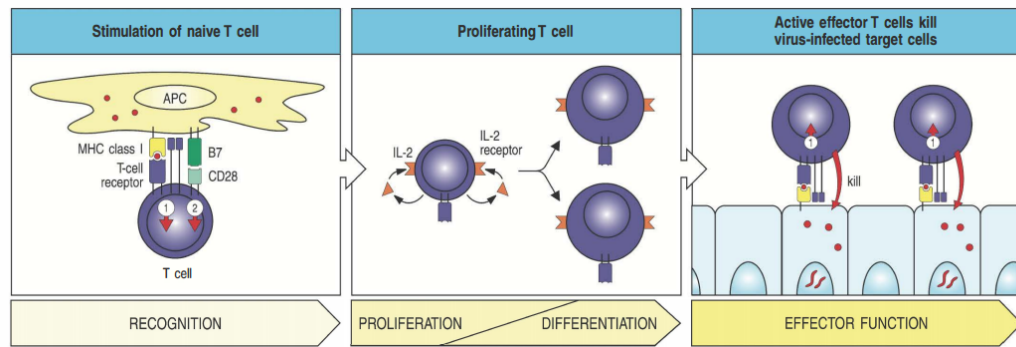


Figure 5 | Stimulation and activation of CD8 T cells. (A) A naïve T cell recognizes a specific antigen on an antigen presenting cell (APC) and gets activated through the TCR:antigen interaction and co-stimulation of CD28. (B) The activated cell produces IL-2 and drives its own clonal expansion, and finally differentiates into an effector cell phenotype. (C) The effector cells are able to recognize and kill target cells that present the specific antigen without the need for co-stimulation (adapted from Janeway's Immunology¹).

production of IL-2, with which the T cell stimulates its own proliferation⁵⁰ (Fig. 5B). Different co-stimulatory signals can be provided by inducible co-stimulator ICOS or CTLA-4 (CD152), which are both related to CD28. Like CD28, both also bind B7 molecules, but while ICOS ligation regulates the production of cytokines, CTLA-4 even restricts the production of IL-2 and therefore serves as a negative regulator of T cell proliferation. Other co-stimulatory molecules, like CD27, 4-1BB (CD137) or OX40 belong to the family of tumor necrosis factor receptor (TNFR) molecules. They stimulate T cell proliferation through triggering of transcription factor NF κ B, which plays a key role in regulating the immune response.^{51,52} After a period of proliferation, activated T cells start to differentiate into effector cells. Most importantly, these effector cells are independent of co-stimulation from now on. If an effector T cell encounters a target cell presenting the antigen for the T cells TCR, it can exert its effector functions quickly and kill the infected target cell (Fig. 5C).⁵³ Also, effector T cells change the expression pattern of their surface molecules. For example, expression of LFA-1 and the integrin VLA-4 is increased.^{54,55} These molecules increase the avidity of T cells for their target cells and ensure that effector T cells can properly home to sites of infection and inflammation, respectively. Furthermore, effector T cells show decreased surface expression of L-selectin (CD62L), and are thereby prevented to circulate through lymph nodes again.⁵⁶ When in contact with target cells, CD8 T cells quickly form immunological synapses that allow them to carry out their effector functions.

1.3.2 Formation of the cytotoxic T cell immunological synapse, and CD8⁺ T cell effector functions

When recognizing a target cell that presents the specific peptide for the effector CD8⁺ T cell, the T cell forms a cell to cell contact, called the immunological synapse (IS).^{45,57,58} There, the TCR and its co-receptors cluster and give rise to the so called supramolecular activation complex (SMAC). Other surface molecules are recruited to the site, and build a circle around the central zone, that is comprised of TCR-microclusters (TCR-MC) and its co-receptors, called central SMAC (cSMAC). Accordingly, the more distant areas are called peripheral SMAC (pSMAC), where LFA-1 is located, and distal SMAC (dSMAC, Fig.6).⁵⁸ Integrin LFA-1, and its strong binding to ICAM-1 play a vital role in the creation of this contact site. At the same time, the cytoskeleton is restructured, and the T cell gets polarized. A pivotal component of this reorganization process is Wiskott-Aldrich syndrome protein (WASP), that is activated by adapter protein Nck or GTP-binding proteins CDC42 and Rac1. When the T cell is polarized, actin accumulates at the cell to cell-interface, and later is reorganized into the dSMAC ring.⁵⁸ Also, in a step by step process, the microtubule-organizing center (MTOC) or centrosome, reorientates towards the synapse, and so do the cytolytic granules, which are then released towards the target cell.⁵⁷⁻⁶² Cytolytic granules are a special form of lysosomes, that can contain different types of cytotoxic effector molecules. Notably, these effector molecules are stored in their active form, rendering them potentially dangerous also for the effector cell itself. However, pH controlled conditions in the granules prevent them from causing damage to any other than the target cell. In CD8⁺ T cells, cytolytic granules usually contain perforin, granzymes and granulysin. Perforin is a pore-forming protein that acts both on the target cell membrane and on the membrane of the granules, allowing entry of cytolytic proteins into the target cell.⁶³ Granzyme are a group of serine proteases, that are mostly described for inducing apoptotic pathways in the target cell,⁶⁴ while granulysin additionally has antimicrobial activity.⁶⁵

Also, granules can contain cytokines that shape the immune response.⁶⁶ The most prominent cytokine for CD8⁺ T cells is interferon- γ (IFN- γ). It can directly inhibit viral replication or remove virus particles from infected cells. Also, IFN- γ recruits and activates other immune cells, like macrophages and neutrophils.⁶⁷ CD8⁺ T cells can also release different interleukins, like IL-2 and IL-3 or TNF- α . However, CD4⁺ effector T cells are a far more powerful producer of immune shaping cytokines. Importantly, cytotoxic effector T cells can also express effector molecules bound to their membranes, among those Fas ligand or TNF- α . When Fas ligand interacts with Fas that is presented by the target cell, target cell apoptosis is induced by a subsequent signaling cascade.⁶⁸ Membrane-bound TNF- α can also induce apoptosis when

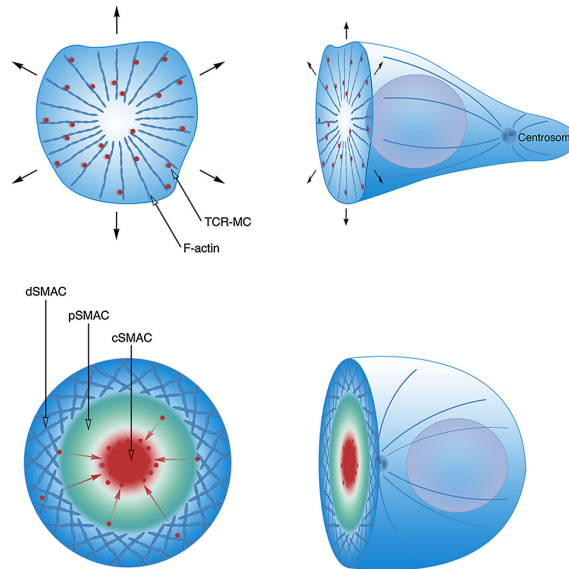


Figure 6 | Formation of the immunological synapse. Schematic displays IS initiation (top) and maturation (bottom), from perspective of the target cell (left) and the side (right). Filamentous actin accumulates at the IS, and drives TCR-microclusters into the pSMAC. Integrins like LFA-1 cluster in the pSMAC, while f-actin is reorganized into the dSMAC ring. Also, the MTOC or centrosome relocates from the distal part of the cell to the IS (adapted from Le Floch and Morgan⁵⁸).

interacting with a TNF-receptor on the target cell, like TNFR-I.⁶⁹

1.4 Mucosal-associated invariant T cells

1.4.1 Phenotype of MAIT cells

Usually, different T cell clones express a variety of different T cell receptors (TCR), that recognize a huge diversity of antigen:MHC complexes. However, in recent years T cell subsets have been characterized that express invariant or semi-invariant TCRs and are therefore restricted to the recognition of certain target molecules.⁷⁰ The first identified invariant T cell subset expresses an invariant T cell receptor with a unique TCR α -chain, consisting of TRAV10 (V α 24) and TRAJ18 (J α 18) segments, and is now known as the invariant NKT (iNKT) cell subset.⁷¹ To current knowledge, these T cells only recognize lipid and glycolipid antigens that are presented by CD1d, and display features distinct from CD4 and CD8 T cells.⁷² More recently, a T cell subpopulation has emerged that expresses the TRAV1-2 (V α 7.2) and TRAJ33 (J α 33) segments in humans, and TRAV1 (V α 19)/TRAJ33 (J α 33) in mice. This new subset was first identified as part of the double negative (DN) CD4⁺CD8⁻ T cells, found to be conserved in humans, mice and cattle and abundant in the gut lamina propria.⁷³ They were

therefore named mucosal-associated invariant T (MAIT) cells and are also highly abundant in blood and liver. There, these cells make up 1-10 % and 20-45 % of the whole T cell population, respectively.^{74,75} In mice however, MAIT cells are only 0.1 % of T lymphocytes in the peripheral blood.⁷⁶ Human MAIT cells are generally defined as T cells that express the V α 7.2 segment of the TCR, and have also been shown to express high levels of IL-18 receptor (IL18-R α).^{77,78} In humans, most MAIT cells are either CD8 $\alpha\alpha$, CD8 $\alpha\beta$ or DN T cells, with only a small proportion expressing CD4,⁷⁹ and display an effector (CD95^{hi}CD62L^{lo}) memory (CD27⁺CD45RO⁺CD45RA⁻CD122⁺) phenotype in adult human blood.⁸⁰ They also express high levels of CD26, multi drug resistance protein 1 (MDR1),⁸⁰ the receptors for interleukins 12, 18 and 23, and chemokine receptors CCR6, CCR5, CCR9 and CXCR6.^{76,80,81} Dipeptidyl peptidase-4 or CD26 has just recently been described as a MAIT cell specific marker,⁸² and is usually associated with activated and memory T cells.^{83,84} MDR1 is associated with drug efflux, and might reflect the diverse toxins present in the MAIT cell environment.⁷⁸ It also allows MAIT cells to survive chemotherapy against acute myeloid leukemia and breast cancer,^{80,85} and is additionally associated with long lifespans.^{86,87} Expression of interleukin receptors allows MAITs to be specifically activated by cytokine stimulation, which significantly distinguishes them from other T cell types.⁷⁸ Chemokine receptors CCR6 and CXCR6 that are expressed by MAIT cells enable them to traffick to intestine and liver,^{88,89} where they make up the predominant T cell subpopulation.⁸⁰ Notably, MAIT cells also express high levels of CD161 (NK1.1), a feature shared with NKT cells.^{77,80} CD161 is a C-type lectin (Ilanier 1994 NKR-P1A), and expressed by NK cells and a proportion of T cells,⁸⁰ out of which MAIT cells represent the majority.⁹⁰ However, the exact function of CD161 is still under debate. On NK cells, CD161 acts as an inhibitory receptor upon interaction with its ligand.^{91,92} On T cells the situation is less clear. While one group reported no effect of linking CD161 on anti-CD3/CD28 stimulation,⁹² results from a different publication suggest increased expression of IFN- γ upon CD161 triggering.⁹³ Furthermore, a recent study has reported that ligation of CD161 decreases MAIT cell cytokine production, but not cytotoxicity.⁹⁴ The transcription of MAIT cell genes is suggested to be hugely influenced by high expression of transcription factors ROR γ t and PLZF (ZBT1B6),⁹⁵ high abundance of the latter being a feature MAIT cells share with NKT and $\gamma\delta$ T cells.^{96,97} Notably, PLZF is absent in conventional T cells and might be a master transcription factor for MAIT cells.⁹⁸ Retinoic acid-related orphan receptor γ t (ROR γ t) has been shown to be associated with high expression of CD161 and a marker for T cells that secrete IL-17.^{90,99}

In summary, MAIT cells are a recently discovered T cell subpopulation that is highly abundant in liver, gut and the peripheral blood.^{7,78,98,100} They express a semi-invariant T cell receptor, tissue-homing markers and receptors for different interleukins (Fig. 7). Furthermore,

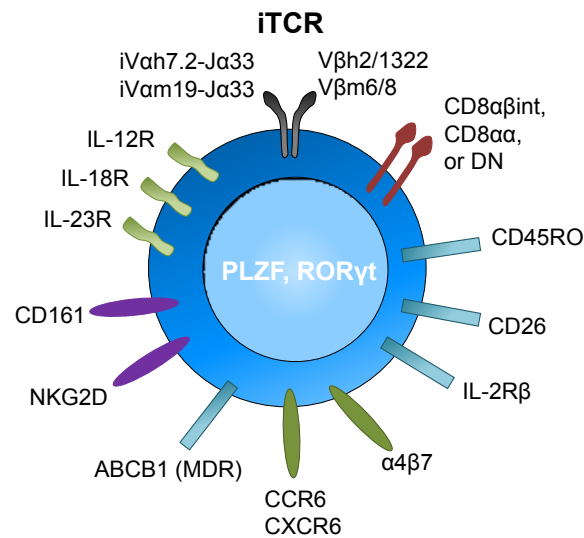


Figure 7 | Surface markers and transcription factors of a typical, adult MAIT cell. MAIT cells express a semi-invariant T cell receptor that contains the V α 7.2 segment. They also express tissue homing receptors, receptors for interleukins and markers of memory T cells. Furthermore, all MAIT cells express high levels of CD161 and MDR1, and most of them are CD8-positive. Important transcription factors for MAIT cell development are ROR γ t and PLZF, that are highly abundant in that subset (adapted from Le Bourhis *et al.*¹⁰⁰).

high expression of NK cell-associated receptor CD161 is a trademark of MAIT cells. That feature is usually associated with IL17-secreting T cells, and so is the presence of transcription factor ROR γ t. Another prominent transcription factor in MAIT cells is PLZF, that is also present in the semi-invariant NKT cell subset and absent in conventional T cells.

1.4.2 Activation and function of MAIT cells

Until 2010, the exact function of MAIT cell was not well understood. Then, in that particular year two studies were published that observed MAIT cells to exert antimicrobial activity against a wide variety of bacteria and yeasts, but not viruses.^{79,101} Gold and colleagues reported that MAIT cells were able to respond to *Mycobacterium tuberculosis* infections, even if the host had not encountered this bacterium before.¹⁰¹ Also, MAIT cell activation by *Escherichia coli*, *Salmonella typhimurium* and *Staphylococcus aureus* was observed. The second paper, written by Le Bourhis and colleagues reported anti-microbial activity of MAIT cells against monocytes that had been fed with *E. coli* or other bacteria, like *S. aureus* or *Pseudomonas aeruginosa*.⁷⁹ Notably, not all bacteria could induce MAIT cell activation. For example, incubation with *Enterococcus faecalis* did not lead to anti-microbial responses. Additionally, some yeasts like *Candida albicans* were able to activate MAIT cells. This activity was dependent on MHC-class

I-related molecule MR1. MAIT cells have been found to be restricted by MR1, and are absent in MR1 knockout mice.⁸¹ Notably, MR1 is the most conserved MHC class I or MHC class I-related molecule between mice and humans,¹⁰² sharing up to 89 % sequence homology, especially in the ligand binding groove. This implies strong evolutionary pressure, leading to very stringent amino acid conservations of this MAIT-restricting protein. The antigens that are presented by MR1 have been identified just recently, and have already been suspected to be a conserved microbial product. Investigations revealed that the antigen could neither be cleaved by proteases, nor did it copurify with lipids.^{103,104} In 2012, refolding experiments of MR1, and subsequent mass spectrometry analyses revealed vitamin B metabolites as ligand for MR1.¹⁰⁵ This study therefore presented a whole new class of antigen for MHC-like molecules and the immune system. However, the structures with the highest affinity to MR1, a derivative of folic acid, did not activate MAIT cells. As *S. typhimurium* is described to induce MAIT cell activation,¹⁰¹ it was assumed that *S. typhimurium* supernatant would induce refolding of MR1, indicating the formation of an MR1:ligand complex. Indeed, along with synthetic ligand that can bind MR1 and activate MAITs, several metabolites from the synthesis pathway of vitamin B2 (riboflavin) were identified to refold MR1, and the built complex activated MAIT cells (Fig. 8).¹⁰⁵ Strikingly, this is consistent with the observation that all MAIT-activating microorganisms have a functional pathway for riboflavin synthesis. Accordingly, all bacteria lacking this pathway are not able to induce MAIT cell activation - and so are mammals, as they are not able to synthesize riboflavin. However, the biochemical origin of the identified synthetic ligand, which displayed the strongest activating stimulus of all activating compounds, could not be determined. Later, analysis of MAIT cell activation through *Lactococcus lactis* strains with mutations of specific riboflavin synthesis pathway proteins revealed early riboflavin synthesis intermediate product 5-amino-6-D-ribitylaminouracil (5-A-RU) to be a pivotal molecule in MAIT cell activation.¹⁰⁶ Although 5-A-RU itself is unable to bind MR1 or activate MAIT cells directly, it can condensate non-enzymatically to unstable products that can covalently and reversibly bind MR1. Interestingly, one of these products in complex with refolded MR1 displayed the same mass as the synthetic ligand identified in the previous study,¹⁰⁵ suggesting this to be the true ligand for MR1.¹⁰⁶ Furthermore, in various bacterial strains different abundances of MR1:ligand complexes were found, indicating that different bacteria might be able to produce diverse ligands that activate MAIT cells. Most recently it was also discovered that certain compounds can actually competitively inhibit MAIT cell activation by binding MR1.¹⁰⁷

Although MAIT cell activation is of course also dependent of TCR signaling, some studies have reported that especially adult MAIT cells are rather responsive to stimulation that are TCR-independent.^{76,80,85} However, co-stimuli like CD28 or cytokines like IL-12 and IL-18 can

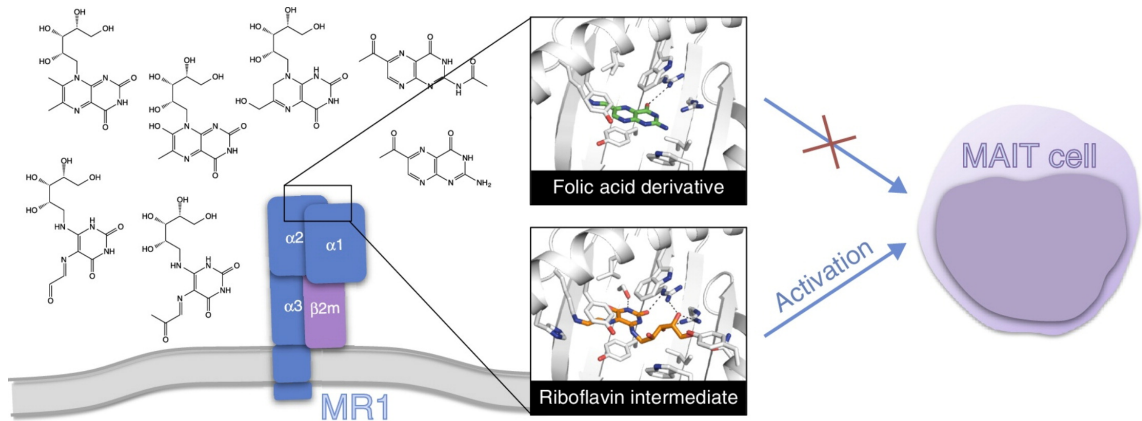


Figure 8 | Presentation of riboflavin metabolites activates MAIT cells. MR1 refolds in the presence of several chemical compounds, among them pterines, lumazines and pyrimidines (left). Not all of them, however, lead to the activation of MAIT cells. Only riboflavin intermediates are able to trigger MAIT cell effector functions (adapted from McWilliams *et al.*¹¹⁹).

overcome this lack of responsiveness.¹⁰⁸ Especially the responsiveness to innate cytokines like IL-12 and IL-18 is similar to NK cells.¹⁰⁹ For example, innate signaling via toll-like receptor 8 is a potent trigger for production of IL-12 and IL-18 and might therefore passively activate MAIT cells in viral infections, where they can produce IFN- γ .^{110,111} This would also explain the presence of MAIT cells during other pro-inflammatory settings that are not associated with bacterial infection.^{112–116} Upon activation, MAIT cells readily produce cytokines like IFN- γ , TNF- α and IL-17 (Fig. 9).^{77,80} Additionally, MAIT cells have been observed to efficiently lyse bacterially infected cells, and express perforin and granulysin,⁹⁴ as well as granzyme A and B.^{79,80,101} A recent study also indicated that expression of granzyme B and perforin increases after activation, and therefore cytotoxic capacity is enhanced.¹¹⁷ Importantly, MAIT cells are innately pathogen reactive. Even when being inexperienced, and not having been exposed to antigen, MAIT cells have the capacity to respond to bacterial infections.¹¹⁸ This immediate functional reaction to new pathogens never encountered before is a key feature of innate immune cells.

Overall, MAIT cells are restricted by MR1. Antigens that in complex with MR1 activate MAIT cells have just recently been discovered. These antigens are small compounds, indicating a new class of antigens for T cells, and are associated with the riboflavin synthesis pathway. MAIT cells can also be activated by cytokines, and exert cytotoxic activity as well as the release of cytokines, predominantly IFN- γ and IL-17. They are even capable of immediately displaying effector functions without being exposed to the antigen before, a clear feature of innate immune cells.^{7,78,119}

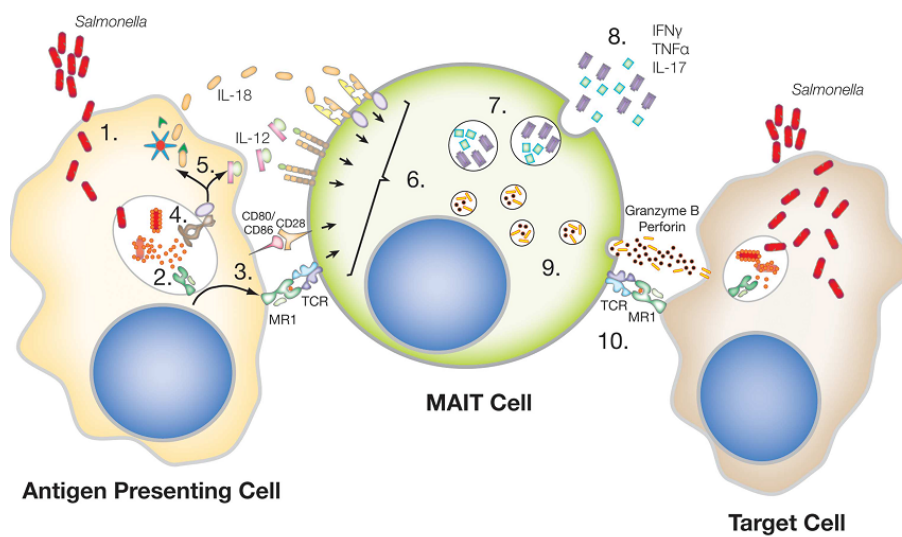


Figure 9 | MAIT cell effector functions. Bacteria are internalized by APCs and the MAIT cell antigen, which is converted out of 5-A-RU binds to MR1. MR1 translocates to the cell surface, and is presented in combination with co-stimulatory receptors. TLRs recognize other bacterial parts and lead to the release of cytokines like IL-12 and IL-18. One of these mechanisms then activates the MAIT cell, which then expresses and secretes cytokines IFN- γ , TNF- α and IL-17. Also, expression of granzyme B and perforin is increased in MAIT cells and can lead to the death of the target cell (adapted from Ussher *et al.*⁷⁸)

1.4.3 Development of MAIT cells

Like other T cells, MAIT cells develop in the thymus, where they arise from uncommitted DN precursors (Fig. 10).^{6,73,76,120} There, an endogenous ligand for MR1 has been suggested on hematopoietic cells that select MAIT cells,^{76,81} as MR1 has been shown to be expressed on CD3⁺CD45⁺ hematopoietic T cells.¹¹⁸ As murine MAITs are selected by double positive thymocytes,¹²¹ this might also be true for human MAITs. The need for a specific educational program for MAIT cells in the thymus becomes apparent when considering that the MAIT cells found in cord blood are already displaying a phenotype distinct from conventional T cells,^{76,95,118} with high expression of CD161 and IL-18 receptor.^{76,80} Also, MAIT cells already express transcription factors ROR γ t and PLZF.⁹⁵ The abundance of this transcription factors is shared with innate-like NKT cells and $\gamma\delta$ T cells, suggesting a shared developmental pathway.^{96,97} However, MAIT cells exit the thymus as naïve cells, unlike NKT cells.¹²⁰ In the mucosal tissues of the fetus, MAIT cells mature without the influence of the commensal flora or other microorganisms. This maturation process is associated with the acquisition of PLZF expression.¹²⁰ Interestingly, and contrary to NKT cells, this process seems to be independent of the SLAM/SAP pathway, as reportedly the number of MAIT cells was normal

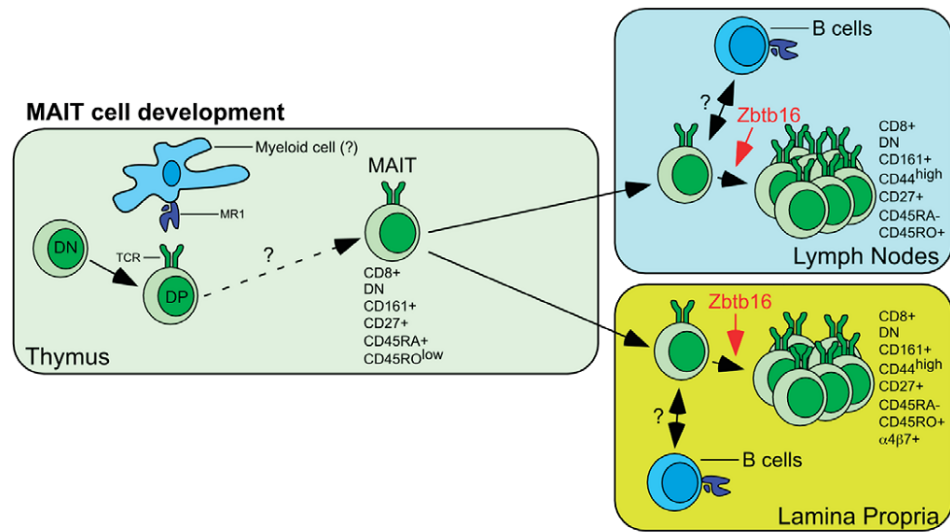


Figure 10 | Schematic view on MAIT cell development. In the thymus, DN precursors give rise to MAIT cells. They acquire expression of the invariant T cell receptor and are most likely selected by CD3⁺CD45⁺ hematopoietic T cells. The details of the maturation process, however, are still unclear. MAIT cells then leave the thymus, displaying a naïve phenotype (CD45RA⁺CD45RO^{low}), and expand in the periphery upon interaction with B cells (adapted from Gopin⁶).

in SAP-deficient patients.⁷⁶ Also, MAIT cells that are deficient of SAP express PLZF at normal levels. Once MAIT cells reach the peripheral tissues, they expand rapidly in a B cell dependent manner.⁷⁶ This expansion is also dependent on the commensal flora. Accordingly, MAIT cells are absent in germ-free mice, as well as in mice lacking B cells.^{76,81}

1.4.4 MAIT cells and diseases

The role of MAIT cells in human diseases has not been fully elucidated to that point.^{7,78} In mouse models of infections, where mice were infected with *Escherichia*, *Mycobacteria*, *Klebsiella* and *Francisella*, the absence of MAIT cells directly correlated with increased bacterial load.^{79,122–124} Also human patients that suffered from bacterial infections like *M. tuberculosis* have shown decreased numbers of MAIT cells,^{79,101,125,126} an observation that correlates with an increase in susceptibility for secondary infections in critically ill patients.¹²⁷ Interestingly, also in HCV and HIV infections, MAIT cells are depleted in peripheral blood.^{77,128,129} In HCV infections, the decrease in numbers can be attributed to the movement of MAIT cells towards the liver, where they are suggested to assume a protective role.⁷⁷ During HIV infection, the loss of MAIT cells from the peripheral blood has been described to be early and irreversible, and numbers do not recover even in patients where anti-retroviral therapy

is successful.^{125, 128, 129} Either activation induced cell death¹²⁹ or downregulation of CD161 and exhaustion¹²⁸ have been suggested to be responsible for this depletion. Strikingly, MAIT cells also seem to play a role in non-infectious diseases. For example, increased MAIT cell numbers have been reported in the brains of multiple sclerosis patients,^{114, 130} and patients suffering from inflammatory bowel disease show increased numbers of MAIT cells in the inflamed tissue.¹¹⁶ It is therefore likely that MAIT cells locate from the blood to the inflamed tissues in the body, and has shown also to be the case in psoriasis, rheumatoid arthritis and experimental autoimmune encephalomyelitis.^{77, 113, 115, 131} Also, MAIT cells have been reported to be recruited to kidney and brain tumors.¹³²

Taken together, MAIT cells seem to play a role not only in the control of bacterial infections, where they assume protective roles and decrease susceptibility to secondary infections. They are also affected in the course of viral infections like HIV and HCV, although they have not been shown to be activated by viruses until now. Furthermore, MAIT cells also infiltrate inflamed tissue in auto-inflammatory diseases, and tumors.

1.5 Aim of thesis

Innate immune cells comprise a crucial part of our immune system. Without this first line of defense, survival for any species would hardly be possible, as this quick response to pathogen invasion not only fends off most of the invading pathogens itself, but also provides activating stimuli for the later, adaptive response. Overall, the aim of this thesis was to shed light on novel mechanisms of innate immunity, and reveal how the activity of fundamentally different immune cells is realized.

Natural killer (NK) cells are an important part of the innate defense, and mediate protection against virus-infected cells, tumors, but also bacteria. Furthermore, they also modulate the immune response by killing active immune cells and releasing pro-inflammatory cytokines. Their activity is regulated by a variety of germline-encoded receptors, but the signaling network that is triggered by engaging these receptors is incompletely understood. Recently, a proteomic study has identified a number of kinases that are promptly phosphorylated after NK cell activation and are therefore directly involved in NK cell activity, among them Fyn, CaMKII and PKD.⁴³ However, the physiological role of these kinases has never been assessed. Thus, activity of primary human NK cells that are isolated from human donor blood will be evaluated after perturbing the activity of Src kinases, CaMKII and PKD. These data will allow further characterization of the role of these kinases in NK cell signaling, and preferentially reveal effects that are independent of the donor.

During the course of these experiments, a new cell type with innate properties came into focus of the research community. Mucosal-associated invariant T (MAIT) cells recognize a new class of bacterial ligand and are able to fight infections without prior activation. Although in recent years MAIT cells have been subject to a number of studies, their exact function is still unclear and their functional inventory undefined. Recent studies have shown that systematic techniques like proteomics are ideal to define conserved features in different immune cell subsets.¹⁹ It was therefore decided to compare the proteome of primary human MAIT cells with NK cells and CD8⁺ T cells, as both of these cell types are prototypic for innate and adaptive immunity, respectively. Also, both NK and CD8⁺ T cells share features with MAIT cells. Thus, this kind of analysis will allow investigation of the differences between MAIT cells and conventional adaptive T cells, and reveal novel mechanisms through which MAIT cells realize their innate function. Also, the repertoire of MAIT cell effector molecules can be defined, and typical features of the MAIT cell phenotype will be characterized.

Furthermore, the MAIT immunological synapse will be investigated for the first time. Although the effector functions of MAIT cells have been thoroughly investigated in the last years, the interface between MAIT cell and target cell was never addressed in detail.

2 Material and Methods

2.1 Equipment and software

2.1.1 Equipment

autoMACS Pro Separator, Miltenyi Biotec

BD Accuri C6 Flow Cytometer, Accuri Cytometers Inc.

BD LSR II Flow Cytometer, BD Biosciences

BD FACSAria II SORP Cytometer, BD Biosciences

Innova CO-170 CO₂ incubator, New Brunswick Scientific

Multifuge 1 S-R, Heraeus

Inverted microscope Ti-E, Nikon

MoFlo XDP cytometer, Beckman Coulter

Orbitrap Fusion, Thermo Scientific

LTQ Orbitrap Velos Fourier Transform, Thermo Scientific

RC10101 SpeedVac, Sorvall

Sorvall Discovery MS120SE ultra centrifuge, Hitachi

Ultimate 3000 HPLC, Dionex

2.1.2 Software

BD Accuri CFlow Sampler 1.0.264.21, Accuri Cytometers Inc.

BD Accuri CFlow Analysis Plus 1.0.264.21, Accuri Cytometers Inc.

Chromeleon 6.8, Dionex

FACSDiva 6.1, BD Biosciences

FlowJo 10.0.7, TreeStar Inc.

Mascot Server 2.4.1, Matrix Science

MetaCore GeneGo pathway analysis, Thomson Reuter

Microsoft Excel 2010, Microsoft

NIS-Elements AR 4.30.20, Nikon

Pathway Studio 11.0.0.1, Elsevier

ProteomeDiscoverer 1.4.1.14, Thermo Scientific

RStudio 0.98.994, RStudio Inc.

Xcalibur software suite 3.0.63, Thermo Scientific

2.2 Chemicals, buffers and media

If not indicated otherwise, all used chemicals were obtained from the following companies: PAA Laboratories (Pasching, Austria), Life Technologies/Invitrogen/Gibco (Carlsbad, CA, USA), Sigma-Aldrich/Fluka (St. Louis, MO, USA), Carl Roth GmbH (Karlsruhe, Germany) and BD Biosciences (Franklin Lakes, NJ, USA). All buffers and solutions were prepared with ultra pure water, obtained from a MembraPure Astacus purification system (Membrapure GmbH, Bodenheim, Germany).

2.2.1 Buffers

Cysteine blocking reagent: Isopropanol with 200 mM methyl methanethiosulfonate (MMTS)

DDM lysis buffer: 50 mM HEPES, 15 mM NaCl, 1 % cOmplete Protease Inhibitor Cocktail (Roche), 1 % dodecyl-maltoside

Dissolution buffer: 1 M tetraethylammonium bromide (TEAB)

FACS buffer: PBS supplemented with 2 % FBS and 2 mM ethylenediaminetetraacetic acid (EDTA), sterile filtered

FACS permeabilization solution: FACS buffer supplemented with 0.5 % saponin

Fixation solution: PBS supplemented with 2 % paraformaldehyde (PFA)

GolgiPlug/GolgiStop-solution: RPMI complete supplemented with GolgiPlug (BD Bioscience) diluted 1:100 and GolgiStop (BD Bioscience) diluted 1:150

IF permeabilization solution: PBS supplemented with 0.15 % Triton-X

IF blocking solution: PBS supplemented with 1 % bovine serum albumin (BSA), 0.1 % Tween-20

IF washing solution: PBS supplemented with 0.1 % Tween-20

Isolation buffer: Phosphate buffered saline (PBS) supplemented with 4% fetal bovine serum, sterile filtered

MS buffer A: 0.1 % formic acid

MS buffer B: 0.1 % formic acid, 80 % acetonitrile

PBS: 1.37 mM sodium chloride, 2.7 mM potassium chloride, 12 mM phosphate ($\text{HPO}_4^{2-}/\text{H}_2\text{PO}_4^{2-}$)

Reducing reagent: 50 mM tris(2-carboxyethyl)phosphine (TCEP)

RP buffer A: 0.2 % trifluoroacetic acid (TFA), 3 % acetonitrile (ACN)

RP buffer B: 0.2 % trifluoroacetic acid, 60 % acetonitrile

SCX buffer A: 25 % acetonitrile, 0.065 % formic acid

SCX buffer B: 25 % acetonitrile, 0.065 % formic acid, 500 mM potassium chloride

Urea lysis buffer: 1 M tetraethylammonium bromide (TEAB) supplemented with 8 M urea

2.2.2 Media

Lysogeny broth: 15 g/L yeast extract, 10 g/L tryptone, 7 g/L sodium chloride

LB agar: LB medium with 15 g/L agar

RPMI complete: RPMI 1640 (PAA) supplemented with 10 % FBS (PAA), 1 % Penicillin/Streptomycin and 1 % L-Glutamine

RPMI K562: RPMI 1640 (PAA) supplemented with 10 % FBS (PAA), 1 % Penicillin/Streptomycin

Table 1 | Small molecule kinase inhibitors.

name	target kinase	manufacturer	concentration range
CID755673	PKD	Tocris Bioscience	5 μ M - 200 μ M
CK59	CaMKII	Merck	10 μ M - 200 μ M
Dasatinib	SFK/Fyn	LC Laboratories	10 nM - 300 nM

Table 2 | Used cell lines

name	origin	reference name
K562	chronic myelogenous leukemia	ATCC CCL-243 TM
THP-1	acute monocytic leukemia	ATCC TIB-202 TM

2.2.3 Kinase inhibitors

Kinase inhibitors used in this study are shown in table 1. The inhibitors were purchased from LC Laboratories (Woburn, MA, USA), Merck KGaA (Darmstadt, Germany) and Tocris Bioscience (Ellisville, MO, USA). Dasatinib was stored at -20°C, CID755673 and CK59 at 4°C. All inhibitors were solubilized in dimethyl sulfoxide (DMSO) and diluted with PBS as indicated.

2.3 Cells

Primary peripheral blood mononuclear cells (PBMCs) were isolated from the peripheral blood of healthy human donors. Buffy coats were kindly provided by the Deutsches Rotes Kreuz (NSTOB Springe). Used cell lines are shown in Table 2.

2.4 Antibodies

Monoclonal antibodies (mAbs) used for flow cytometric analyses are shown in Table 3. For immunofluorescence experiments, primary antibodies as well as fluorochrome-conjugated secondary antibodies were used. These antibodies are shown in Tables 4 and 5, respectively.

Table 3 | Antibodies used for flow cytometry.

antigen	isotype	clone	conjugate	manufacturer
CD3	mouse IgG2a	BW264/56	FITC	Miltenyi
CD3	mouse IgG2a	HIT3a	PE	BD Bioscience
CD8	mouse IgG1	RPA-T8	PE	BD Biosciences
CD14	mouse IgG2b	M ϕ P9	APC-Cy7	BD Biosciences
CD19	mouse IgG1	SJ25C1	APC-Cy7	BD Biosciences
CD48	mouse IgG1	BJ40	FITC	BioLegend
CD56	mouse IgG1	AF12-7H3	APC	Miltenyi
CD56	mouse IgG1	HCD56	PE-Cy5	BioLegend
CD69	mouse IgG1	L78	PE	BD Biosciences
CD98	mouse IgG1	MEM-108	FITC	BioLegend
CD107a	mouse IgG1	H4A3	PE	BioLegend
CD161	mouse IgG1	DX12	APC	BD Biosciences
IFN- γ	mouse IgG2b	25723.11	FITC	BD Biosciences
TNF- α	mouse IgG1	MAb11	eFluor 450/PacificBlue	eBioscience
V α 7.2	mouse IgG1	3C10	PE-Cy7	BioLegend

Table 4 | Primary antibodies used for immunofluorescence.

antigen	isotype	clone	manufacturer
CD107a	rabbit IgG1b	N/A	Cell Signaling
CD107a	rabbit IgG	polyclonal	Abcam
perforin	mouse IgG2b	δ G9	BD Biosciences
α -tubulin	rat IgG1	37B5	Synaptic Systems
S100A4	rabbit IgG1	EPR2761(2)	LifeSpan Biosciences
secernin-1	rabbit IgG	polyclonal	Synaptic Systems

Table 5 | Seconday antibodies used for immunofluorescence.

name	reactivity	species	conjugate	manufacturer
A12c	anti-mouse	goat	Alexa Fluor 488	Invitrogen
A13c	anti-mouse	goat	Alexa Fluor 594	Invitrogen
B11c	anti-rabbit	goat	Cy5	Dianova
B12c	anti-rabbit	goat	Alexa Fluor 488	Invitrogen
B13c	anti-rabbit	goat	Alexa Fluor 594	Invitrogen
-	anti-rat	goat	Alexa Fluor 647	
C12c	anti-rat	goat	Alexa Fluor 488	Invitrogen
C13c	anti-rat	goat	Alexa Fluor 594	Invitrogen

2.5 Methods of Microbiology

2.5.1 Used bacterial strains

The strain used for activation of MAIT cells was *Escherichia coli* BL21 with the genotype F^- , ompT, hsdS_B, (r_B⁻, m_B⁻), dcm, gal, (DE3) (Novagen).

2.5.2 Cultivation and fixation of bacteria

E. coli were cultivated over night at 37 °C in LB medium free of antibiotics. Bacteria were then plated in different dilutions on LB agar plates, incubated over night and colonies were counted on the next day to determine bacterial concentration. The suspension was then spun down at 10 000×g for 10 minutes, washed with 10 mL PBS, fixated in 5 mL fixation solution for five minutes at RT, washed three times with 10 mL PBS and used directly.

Fixation solution: PBS supplemented with 2

Lysogeny broth: 15 g/L yeast extract, 10 g/L tryptone, 7 g/L sodium chloride

LB agar: LB medium with 15 g/L agar

2.6 Methods of Cell Biology

2.6.1 Culturing of cells

K562 cells were maintained in RPMI K562 medium. Freshly isolated human peripheral blood mononuclear cells (PBMCs), NK cells and THP-1 cells were cultured in RPMI complete medium. All cell types were cultured in culture flasks (Nunc) at a temperature of 37 °C with 7.5 % per volume CO₂, at a maximal density of 6×10^6 cells per mL (PBMCs) and 1×10^6 cells per mL (K562 and THP-1), respectively.

RPMI K562: RPMI 1640 (PAA) supplemented with 10 % FBS (PAA)

RPMI complete: RPMI 1640 (PAA) supplemented with 10 % FBS (PAA), 2 % PenStrep (Gibco) and 1 % L-Glutamine (Gibco)

2.6.2 Isolation of PBMCs from human peripheral blood

Buffy coats from healthy human donors were kindly provided by the Deutsches Rotes Kreuz (NSTOB, Springe). All donors were tested negatively for HIV, HBV and HCV. B-Test Peripheral blood obtained from one buffy coat was equally distributed to 50 mL falcon tubes and diluted with 7.5 mL isolation buffer. Fourteen mL of Biocoll separating solution (Biochrom AG, Berlin, Germany) were covered carefully with this mixture and the tubes were centrifuged at $840 \times g$ for 25 minutes (no deceleration). After centrifugation, the PBMCs were extracted and the cells were spun down ($410 \times g$, 10 minutes) and washed twice with 50 mL isolation buffer. The cell suspension was filtered to remove aggregates and debris (Cell Strainer 40 μ m, Falcon). Subsequently, PBMCs were spun down, resuspended in RPMI medium at a concentration of 6×10^6 cells per mL and processed within two days after isolation.

Isolation buffer: PBS supplemented with 4 % FBS (PAA), sterile filtered

RPMI complete: RPMI 1640 (PAA) supplemented with 10 % FBS (PAA), 2 % PenStrep (Gibco) and 1 % L-Glutamine (Gibco)

2.6.3 Fluorescence activated cells sorting of primary human immune cells

PBMCs were spun down ($300 \times g$, 10 minutes), washed with FACS buffer and stained at a concentration of 2×10^8 cells per mL with respective antibodies in FACS buffer for 15 minutes at 4 °C in the dark. After washing twice with FACS buffer, cells were then sorted with the kind help of Dr. Lothar Gröbe (HZI, Braunschweig). After sorting, cells were pelleted at $840 \times g$ for 20 minutes, frozen at -20 °C and processed further for mass spectrometric analysis (see 2.7).

FACS buffer: PBS supplemented with 2 % FBS (PAA) and 2 mM EDTA (Roth), sterile filtered

2.6.4 Immunofluorescence analysis of MAIT cell activation

PBMCs were spun down (300×g, 10 minutes), washed with FACS buffer and stained at a concentration of 2×10^8 cells per mL with antibodies against CD161 and Vα7.2 for 15 minutes at 4 °C in the dark. Cells were then sorted, with MAIT cells defined as Vα7.2⁺CD161⁺⁺ cells (see Figure 15). Sorted cells were spun down at 300×g for 10 minutes and cultured over night in RPMI complete medium. THP-1 cells were fed with PFA-fixed *E. coli* BL21 (MOI 25) over night and mixed with isolated MAIT cells for the indicated times the next day at a E:T ratio of 1:1. Cells were then transferred to poly-L-lysine cover slips and co-incubated for indicated times. Cells were then fixed in fixation solution for 20 minutes and permeabilized in IF permeabilization solution for 5 minutes. After blocking for one hour in IF blocking solution, samples were stained with primary antibodies and respective secondary antibodies. Samples were washed with IF washing solution three times after each working step. Cover slips were dehydrated with ethanol and subsequently embedded in previously heated moviol. Microscopy was performed on an inverted microscope (Ti-E; Nikon) using standard epifluorescence illumination (light source Intensilight, Nikon) and 100×/1.45 plan-apochromatic immersion oil objective. Images were acquired with a back-illuminated, cooled charge-coupled-device camera (CoolSnap MYO, Roper Scientific). Acquisition was supported by OPTIGRID structural illumination (Nikon) and driven by NIS-Elements AR software (Nikon).

Every image was recorded as a z-stack, allowing in silico 3D reconstruction of the cells as well as maximum intensity projections, displaying the maximum intensities of the layers of the whole z-stack as one 2D image. Also, 3D deconvolution was possible, an algorithm-based technique that removes optical distortion from already acquired images. In brief, a point spread function (PSF) is approximated, that helps to calculate the original light source of every pixel and therefor removes blurring of the image. Deconvolution was carried out over 50 iteration cycles with NIS-Elements AR software, with all parameters adopted from the software.

FACS buffer: PBS supplemented with 2 % FBS (PAA) and 2 mM EDTA (Roth), sterile filtered

Fixation solution: PBS supplemented with 2 % paraformaldehyde (PFA)

IF blocking solution: PBS supplemented with 1 % bovine serum albumin (BSA), 0.1 % Tween-20

IF permeabilization solution: PBS supplemented with 0.15 % Triton-X

IF washing solution: PBS supplemented with 0.1 % Tween-20

RPMI complete: RPMI 1640 (PAA) supplemented with 10 % FBS (PAA), 2 % PenStrep (Gibco) and 1 % L-Glutamine (Gibco)

2.6.5 Flow cytometric analysis of MAIT cell activation

Target cells (THP-1 or primary monocytes) were fed with PFA-fixed *E. coli* BL21 over night (25), and co-incubated with human 500.000 PBMCs for two hours at an E:T ratio of 10:1. In some cases, anti CD28 antibody was added at a final concentration of 1.25 µg per mL. Afterwards, cells were washed with 150 µL FACS buffer, fixed with 100 µL fixation solution (20 min, RT) and stained with monoclonal antibodies (15 min, 4 °C) to be able to exclude non-MAIT cells from the analysis and furthermore assess the activation state. Alternatively, PBMCs were fed with PFA-fixed *E. coli* BL21 directly, incubated for two hours and subsequently fixed, stained and analyzed as described before.

Analysis of MAIT cell activation was conducted on a BD Accuri C6 Flow Cytometer. The flow cytometer operating software was Accuri CFlow Sampler, the compensation matrix was generated with BD Accuri CFlow Analysis Plus. BD CFlow Analysis Plus was also used to analyze data. Additionally, some data points were acquired on a BD LSR II SORP cytometer, operated by FACSDiva software. Data analysis was then carried out by FlowJo.

FACS buffer: PBS supplemented with 2 % FBS (PAA) and 2 mM EDTA (Roth), sterile filtered

Fixation solution: PBS supplemented with 2 % paraformaldehyde (PFA)

2.6.6 Magnetic activated sorting of human NK cells

The primary NK cells were isolated from the cultured PBMCs by magnetic activated cell sorting (MACS) using the NK Cell Isolation Kit (Miltenyi Biotec). The isolation was conducted according to manufacturer's instructions, but only 75 % of the suggested amount of antibodies and magnetic beads were used.

Per isolation 1×10^8 PBMCs were used. PBMCs were spun down ($300 \times g$, 10 minutes), resuspended in 400 µL MACS buffer (Miltenyi) and 100 µL of NK Cell Biotin-Antibody Cocktail (Miltenyi) were added. The cell suspension was incubated at 4 °C for 10 minutes. Afterwards, 300 µL of MACS buffer were added, as well as 200 µL NK Cell MicroBead Cocktail (Miltenyi), and PBMCs were incubated at 4 °C for 10 minutes. After adding 10 mL of MACS buffer, the cells were centrifuged ($300 \times g$, 10 minutes), the supernatant was removed completely and the pellet was resuspended in 500 µL MACS buffer. The cell suspension was filtered (Partec CellTrics 50 µm, Partec, Görlitz, Germany) and NK cells were isolated via autoMACS (Miltenyi) according to the manufacturer's guidelines. The program "DepleteS" was chosen for negative isolation of NK cells. After isolation, the freshly isolated NK cells were resuspended in RPMI complete medium at a concentration of 6×10^6 cells per mL and analyzed within to days after isolation.

RPMI complete: RPMI 1640 (PAA) supplemented with 10% FBS (PAA), 2% PenStrep (Gibco) and 1% L-Glutamine (Gibco)

2.6.7 NK cell degranulation assay

To analyze NK cell degranulation, freshly isolated PBMCs or pure NK cells were used as effector cells. NK cell-susceptible human leukemia K562 cells were used as target cells. Effector cell suspension and target cell suspension were resuspended at 6×10^6 and 12×10^6 cells per mL, respectively. Effector cells were transferred to v-bottomed 96-well plates (100 μ L per well) and respective kinase inhibitors (Tab. 1) were used at the indicated dilutions. Effector cells treated with corresponding amounts of DMSO served as negative controls. Effector cells were incubated with the inhibitors for 15 min at 37 °C.

Afterwards, 50 μ L of the K562 cell suspension were added to a final effector-to-target cell ratio (E:T ratio) of 1:1 (600 000 effector cells and 600 000 target cells per well). Effector and target cells were brought in contact by centrifuging ($30 \times g$ for 3 minutes) and co-cultured at 37 °C for two hours. Subsequently, cells were centrifuged ($450 \times g$ for 3 minutes) and resuspended in 50 μ L FACS buffer containing the fluorochrome-conjugated mAbs shown in table 3. Antibodies were diluted as indicated in table 3. Cells were stained for 15 minutes in the dark at 4 °C.

After staining, cells were washed, resuspended in 100 μ L FACS buffer and subsequently analyzed by flow cytometry.

FACS buffer: PBS supplemented with 2% FBS (PAA) and 2 mM EDTA (Roth), sterile filtered

2.6.8 NK cell cytokine release assay

For the assessment of NK cell degranulation and cytokine release, freshly isolated PBMCs or pure NK cells were used. Human leukemia K562 cells were used as target cells. Effector cells suspension (PBMCs or pure NK cells) were resuspended at 6×10^6 and 1.2×10^6 cells per mL, respectively. Effector cells were transferred to v-bottomed 96-well plates (100 μ L per well) and respective kinase inhibitors (Tab. 1) were used at the indicated dilutions. Effector cells treated with corresponding amounts of DMSO served as controls. Effector cells were incubated with the inhibitors for 15 min at 37 °C.

Afterwards, 50 μ L of the K562 cell suspension were added to a final effector-to-target (E:T) ratio of 10:1 (600 000 effector cells and 60 000 K562 target cells per well). Effector and target cells were co-cultured at 37 °C for one hour. After 17 μ L GolgiPlug/GolgiStop-solution were added, cells were incubated for another five hours. Subsequently, cells were centrifuged ($450 \times g$ for 3 minutes) and resuspended in 50 μ L FACS buffer containing fluorochrome-conjugated mAbs and LIVE/DEAD near IR Cell Stain (Invitrogen). When staining pure NK cells, the mAbs directed against CD14 and CD19 were not added to the staining solution.

Antibodies were diluted as indicated in table 3 and dead cell marker (DCM) was diluted 1:200. Cells were stained for 15 minutes in the dark at 4 °C.

After staining, cells were washed in FACS buffer twice and fixed in 50 µL fixation solution for 10 minutes in the dark. After fixation, cells were resuspended in 25 µL permeabilization solution and incubated for 15 minutes at 4 °C in the dark. For intracellular staining of cytokines, mAbs were diluted in permeabilization solution as indicated and 25 µL of the mixture were added to each well. Cells were incubated for another 30 minutes at 4 °C in the dark. Cells were spun down, washed with FACS buffer and subsequently analyzed by flow cytometry on a BD LSR II SORP cytometer, operated by FACSDiva software. Data analysis was then carried out by FlowJo.

FACS buffer: PBS supplemented with 2 % FBS (PAA) and 2 mM EDTA (Roth), sterile filtered

FACS permeabilization solution: FACS buffer supplemented with 0.5% saponin (Sigma)

Fixation solution: PBS supplemented with 2 % PFA (Sigma)

GolgiPlug/GolgiStop-solution: RPMI complete supplemented with GolgiPlug diluted 1:100 and GolgiStop diluted 1:150 (both BD Bioscience)

2.6.9 Flow cytometric analysis of NK cell degranulation and cytokine release

Analysis of NK cell cytokine release was carried out on a BD LSR II Flow Cytometer (BD Biosciences). The operating system was FACSDiva (BD Biosciences), the necessary compensation matrix was generated with the same software. Here, gating focused on excluding CD14⁺, CD19⁺ and dead as well as adhering cells from the lymphocyte population. The remaining cells were gated on CD3/CD56 characteristics (Fig. 11).

2.7 Semi-quantitative proteomic analysis

2.7.1 Cell lysis and digestion (urea lysis)

Frozen cell pellets were lysed in 50 µL urea lysis buffer per $1 \cdot 10^6$ sorted cells for 30 minutes at RT, with 1 µL of Benzonase added. After incubation, reducing reagent was added 1:10 for 30 minutes, and subsequently cysteine blocking reagent 1:20 for 15 minutes. For protein digestion, combined LysC/trypsin reagent was added at a ratio of 1:20 w/w. After a minimum of 3 hours incubation at RT, the lysate was diluted with H₂O from 8 M to 1 M urea and incubated at 37 °C over night. Peptides were then cleaned up via reverse phase (see 2.7.2). Afterwards, digestion efficiency was checked with a short LC-MS/MS run and a subsequent data analysis of the RAW file with RawMeat software (Vast Scientific). Only

samples containing a high amount of peptides with low numbers of charges were considered as properly digested.

Cysteine blocking reagent: Isopropanol with 200 mM methyl methanethiosulfonate (MMTS)

Urea lysis buffer: 1 M tetraethylammonium bromide (TEAB) supplemented with 8 M urea

Reducing reagent: 50 mM tris(2-carboxyethyl)phosphine (TCEP)

2.7.2 Reverse-phase peptide clean up and desalting

Samples were acidified with 10 % TFA. The pH was checked with pH indicator paper and samples were then centrifuged at $16.000\times g$ for ten minutes. Protein amounts were determined by NanoDrop, samples were then loaded onto according Oasis Extraction Cartridges (Waters), that had before been preactivated, activated and equilibrated with appropriate volumes of pure acetonitrile, RP buffer B and RP buffer A, respectively. After loading the sample twice, columns were washed with RP buffer A twice. Peptide bound to the columns was then eluted with RP buffer B and the eluate was evaporated in the SpeedVac. Afterwards, the whole process was repeated with the sample flowthrough to maximize the yield. After evaporation of the solvent, purified peptides were then frozen at $-20\text{ }^{\circ}\text{C}$ and either labeled with iTRAQTM reagent (see 2.7.3), if already labeled submitted to SCX chromatography (see 2.7.4) or if already fractionated submitted to LC-MS/MS analysis (see 2.7.5). Before labeling or SCX, samples were checked for digestion and labeling efficiency, respectively.

RP buffer A: 0.2 % trifluoroacetic acid (TFA), 3

RP buffer B: 0.2 % TFA, 60 % ACN, 500 mM potassium chloride

2.7.3 Peptide labeling with iTRAQTM

To be able to analyze the samples quantitatively, peptides were labeled with isobaric Tags for Relative and Absolute Quantitation (iTRAQ, Sciex). iTRAQ reagents were heated to RT, solved in 70 μL ethanol and added to generated and cleaned tryptic peptides (see 2.7.1 and 2.7.2, respectively) that had been solved in 30 μL dissolution buffer. One label was used per sorted cell population. The mixture was then incubated at RT for two hours, and evaporated in the SpeedVac. After peptide clean-up to remove excess label reagent (see 2.7.2) and a LC-MS/MS-based check for labeling efficiency, peptide amounts were determined by integration of the total area of all spectra that were detected in the mass spectrometer (Qual Browser, Thermo Xcalibur). Same amounts of differently labeled populations were then combined into one sample that was then submitted to SCX chromatography (see 2.7.4).

Dissolution buffer: 1 M tetraethylammonium bromide (TEAB)

2.7.4 Subfractionation of complex peptide samples through SCX chromatography

To increase the sensitive of mass spectrometric analyses, iTRAQ-labeled and RP-purified samples were fractionated with strong cation exchange chromatography (SCX chromatography). Samples were solved in SCX buffer A and cleaned up by ultracentrifugation at $109.000\times g$ for 20 minutes. Fractions were generated on a Ettan microLC system, using a Mono-S-PC1.6/5-column (both GE Healthcare) with a flow rate of $150\text{ }\mu\text{L}/\text{min}$. To elute the peptides from the column, a linear gradient from 0 % to 35 % SCX buffer B was applied over 15 minutes, while generating one fraction per minute with a microfraction collector (SunCollect). Fractions were combined with regard to the peptide elution profile of the specific samples that could be detected by measuring the absorption at 214 nm with a UV detector. Fractions were then evaporated, desalted (see 2.7.2) and submitted to LC-MS/MS analysis.

SCX buffer A: 25 % acetonitrile, 0.065 % formic acid

SCX buffer B: 25 % acetonitrile, 0.065 % formic acid, 500 mM potassium chloride

2.7.5 Mass spectrometric analyses and data interpretation

LC-MS/MS analyses of purified and desalted peptides were performed on a Dionex UltiMate 3000 n-RSLC system connected to an Orbitrap FusionTM TribridTM mass spectrometer (Thermo Scientific). Peptides of each fraction were loaded onto a C18 pre-column ($3\text{ }\mu\text{m}$ RP18 beads, Acclaim, $75\text{ }\mu\text{m}$ x 20 mm), washed for 3 min at a flow rate of $6\text{ }\mu\text{L}/\text{min}$ and separated on a C18 analytical column ($3\text{-}\mu\text{m}$, Acclaim PepMap RSLC, $75\text{ }\mu\text{m}$ x 25 cm, Dionex) at a flow rate of $350\text{ }\mu\text{L}/\text{min}$ via a linear 120 min gradient from 97 % MS buffer A to 25 % MS buffer B, followed by a 15 min gradient from 25 % MS buffer B to 62 % MS buffer B. The LC system was operated with the Chromeleon software (version 6.8, Dionex) embedded in the Xcalibur software suite (version 3.0.63, Thermo Scientific, Dreieich, Germany). The effluent was electro-sprayed by a stainless steel emitter (Thermo). Using the Xcalibur software, the mass spectrometer was controlled and operated in the “top speed” mode, allowing the automatic selection of as many doubly and triply charged peptides in a three second time window as possible, and the subsequent fragmentation of these peptides. Peptide fragmentation was carried out using the higher-energy collisional dissociation (HCD) mode in the ion trap. MS/MS raw data files were processed via the Proteome Discoverer program (version 1.4, Thermo Scientific) on a Mascot server (version 2.4.1, Matrix Science) using Swiss-Prot/UniProt database. Mascot search parameters used for protein identification are displayed in Table 6. Results were evaluated and quantified using Proteome Discoverer software, with the filters shown in Table 7.

Table 6 | Used Mascot search parameters

parameter	setting
protein database	SwissProt
species	<i>Homo sapiens</i>
enzyme	trypsin
maximum missed cleavage site	1
precursor mass tolerance	10 ppm
fragment mass tolerance	0.05 Da
dynamic modifications	iTRAQ4plex (K)
	iTRAQ4plex (N-term)
	oxidation (M)
static modifications	methylthio (C)
mass precision	2 ppm

Table 7 | Used filters in Proteome Discoverer

filter	setting
peptide confidence	high
search engine rank	1
peptide ion score	30

MS buffer A: 0.1 % formic acid

MS buffer B: 0.1 % formic acid, 80 % acetonitrile

2.8 Statistical evaluation and determination of significantly regulated proteins

Statistical evaluation was performed together with Prof. Dr. Frank Klawonn as described before.¹³³ To identify significant protein regulations the variation of the regulation factors was statistically estimated. In our statistical model we assume that the \log_2 -regulation

factors (RF) of each protein follow a normal distribution ($5 \times 3 \log_2$ RFs per protein due to 5 analyzed donors per immune cell subset comparison) with different expected values, but with the same standard deviation. It is necessary to estimate in order to distinguish significant (donor-independent) deviations from no regulation. The limited number of replicates (5 donors) required an estimation of the standard deviation by taking RFs of all proteins into account. In the used model the mean of the Median Absolute Deviation from the median (MAD) of all proteins serves as an estimator for the standard deviation of a normal distribution (with a correction for small sample sizes). In this way many estimates for the MAD with a large variance are obtained. But averaging this larger number of not very reliable estimates leads to a reliable estimate of the MAD. Based on the previous estimation it is possible to construct a hypothesis test for the identification of significantly regulated proteins. Thereby, the hypothesis of the test encompasses that a protein is considered to be significantly regulated if its mean regulation deviates significantly from 0. The used function represents the cumulative distribution function of the standard normal distribution. A strict test is used, where α is the significance level of the test (here $\alpha = 5\%$; before FDR correction) and where the absolute value of the \log_2 -regulation exceeds a given threshold in at least m ($m = 3, 4, 5$) out of the $k=5$ replicates. n_m is the number of proteins which have been measured in at least m replicates. We used this value for the FDR correction, since we cannot apply the test to proteins that have been measured in less than m replicates. Taken all the parameters together we obtained the value for the threshold as follows:

$$c_\alpha = \sigma_0 \cdot \Phi^{-1} \left(1 - \left(\frac{\alpha}{2 \cdot n_m \cdot \binom{k}{m}} \right)^{\frac{1}{m}} \right)$$

These thresholds (for $m=5$, $m=4$ and $m=3$ donors) were used to define a set of significantly and donor-independently regulated proteins.

3 Results

3.1 The role of Src kinases, CamKII and PKD kinases in NK cell activation

3.1.1 Inhibition of Src kinases, CaMKII and PKD kinases decreases NK cell degranulation and cytokine release in primary human PBMCs

Although NK cells play a pivotal role in the innate defense against viruses and cancer, the signal pathways coordinating their effector functions aren't completely understood. In a recent proteomic study, several kinases were identified to be phosphorylated two minutes after specific NK cell receptor engagement.¹³⁴ Among these kinases were Src family member Fyn, CaMKII and PKD2. To further study the importance of these kinases in NK cell activation, it was decided to investigate NK cell effector functions with the activity of the specific kinases perturbed. Although immortalized cells are easier to manipulate on the level of genes, the use of NK cell lines is only of limited usefulness when assessing effector functions. NK cell lines are usually hyperactive and display a different phenotype from primary material. Therefore, it was decided to use small molecule inhibitors of the specific kinases, and carry out all experiments in primary human material. Specific inhibitors used were Dasatinib (specific for Src family kinases), CK59 (CaMKII) and CID755673 (PKD family kinases). These experiments were partly conducted during a master thesis (Bulitta, 2011), and published later.¹³⁵

The role of Src family kinases, CaMKII and PKD2 in NK cell activation induced by K562 target cells, was assessed by FACS-based methods that have been previously described.¹³⁶ In brief, NK cell activity can be assessed by quantifying degranulation and the release of cytokines. Degranulation can be measured by analyzing the surface expression of CD107a, which appears on the surface after the fusion of cytolytic granules with the membrane.¹⁵ Additionally, intracellular accumulation of cytokines TNF- α and IFN- γ can also be detected by FACS.

Peripheral blood mononuclear cells (PBMCs) were isolated by density gradient centrifugation from human blood of healthy donors. CD3⁺CD56⁺ NK cell populations were then defined by gating PBMCs on lymphocytes, excluding doublets, as well as CD14⁺, CD19⁺

and dead cells (Fig. 11). For activation, PBMCs were co-incubated with K562 target cells, leading to degranulation and cytokine release of NK cells (Fig. 12). To assess the role of the kinases, the specific inhibitors were solved in DMSO and added to PBMCs at indicated concentrations 15 minutes prior to activation with target cells. Pure DMSO added to a mix of NK and K562 cells served as control. Degranulation was then analyzed after 2 hours of co-incubation with K562 target cells. Intracellular accumulation of cytokines was analyzed after 6 hours of co-incubation, and treatment with protein transport inhibitor brefeldin A. Data are presented relative to the DMSO negative controls.

Application of Dasatinib for Src inhibition significantly reduced NK cell degranulation to 50% at a concentration of 150 nM, and led to complete reduction at higher concentrations while having no significant effect at lower doses (Fig. 13A). Additionally, Dasatinib significantly inhibited the production of TNF- α and IFN- γ , even at lowest concentrations. Compared to DMSO controls, the amount of cells positive for TNF- α was reduced to 15 % and IFN- γ production was abrogated almost completely.

Also the application of CK59 (CaMKII inhibition) lead to reduction of NK cell degranulation. However, the effect was more dose-dependent and gradually, while not showing specific dose dependency regarding cytokine production (Fig. 13B). In sum, the effect of CK59 on TNF- α and IFN- γ production was comparable, showing only a moderate reduction at low inhibitor concentrations (10 - 50 μ M). In contrast, higher doses had a significant effect on TNF- α and IFN- γ production, nearly abrogating it at 150 μ M. In total, the effect of CK59 on cytokine release was at higher concentrations even more pronounced than the effect on degranulation.

PKD kinase inhibitor CID755673 also led to a reduction of NK cells degranulation and cytokine release (Fig. 13C). While already 5 μ M CID755673 significantly reduced the amount of degranulating cells, higher concentrations reduced the percentage to 40 % positive cells compared to the controls. Notably, degranulation wasn't reduced further when increasing inhibitor concentrations higher than 50 μ M while an increase of inhibitor concentration to 100 μ M led to pronounced reduction of cytokine release. Production of TNF- α and IFN- γ was also decreased dose-dependently. A dose of 100 μ M CID755673 led to a reduction of TNF- α ⁺ cells to 25 % and IFN- γ production was almost diminished completely at this concentration. Taken together, the application of CD755673 resulted in notable inhibition of NK cell degranulation and cytokine release, and almost completely abrogated IFN- γ accumulation.

In total, treatment of PBMC cultures with Dasatinib, CK59 and CID755673 resulted in significant inhibition of NK cell degranulation and cytokine release. This indicates pivotal roles for the inhibited kinases in mediating activating signals after NK cell stimulation. Furthermore, already in these data donor variations became apparent, with cells of different donors reacting differently to the inhibitor treatment to validate the results, and exclude effects from other

cells in the PBMC cultures it was decided to assess the influence of the inhibitors in purified NK cells.

3.1.2 Donor-specific responses of pure NK cells treated with Dasatinib, CK59 and CID755673

As the experiments described in 3.1.1 were carried out in cultured PBMCs, it couldn't be ruled out that other cells of the culture might have contributed to the observed effects. To validate the inhibitory influence of the compounds and also check for a possible contribution of other cells, all experiments were repeated with pure NK cell cultures.¹³⁵ NK cells were purified by magnetic associated cell sorting (MACS), and subsequently treated with the inhibitor. Activation with K562 target cells, the handling of DMSO controls and flow cytometric analyses were conducted as described before (3.1.1).

Interestingly, for all three inhibitors the variation between individual donors was more apparent when analyzing pure NK cell cultures. This effect was independent of the used inhibitor. Regarding degranulation, the effect by Dasatinib was even more pronounced, completely abrogating it at 100 nM (Fig. 14A). Also, Dasatinib almost completely diminished the amount of cells positive for TNF- α and IFN- γ at the concentration of 50 nM. Interestingly, some donors showed a pronounced increase of cytokine release after this initial reduction. One donor peaked with 30 % positive cells for TNF- α at 200 nM Dasatinib, while another displayed a slight increase at 100 nM. For two donors the amount of IFN- γ -positive NK cells relapsed even further to 60 % positive cells at Dasatinib concentration of 100 μ M and 150 μ M, respectively.

CaMKII inhibitor CK59 also lowered the percentage of CD107a⁺ cells, already decreasing it to 75 % at 100 μ M and nearly complete reduction at 150 μ M (Fig. 14B). Notably, some donors also showed a small increase of degranulation at the lowest concentration of CK59. The inhibitor's effect on TNF- α and IFN- γ release was more pronounced, decreasing the number of cells positive for TNF- α approximately to 25 % at 100 μ M, and reducing it even further at 150 μ M. Again, two donors showed considerably variation from the others, showing an increased response compared with the DMSO controls. The first peaked with 250 % cells positive relative to the control at 20 μ M CK59, which dose-dependently dropped to 20 % at higher concentrations. IFN- γ release was also inhibited dose-dependently in two donors, with one of these showing an increase of positive cells at 10 μ M. Interestingly, the number of IFN- γ ⁺ NK cells increased in two different donors to 140 % at 20 μ M CK59, and decreased at higher concentrations. Another donor even showed a high increase of IFN- γ , that peaked with 340 % positive cells at 50 μ M CK59.

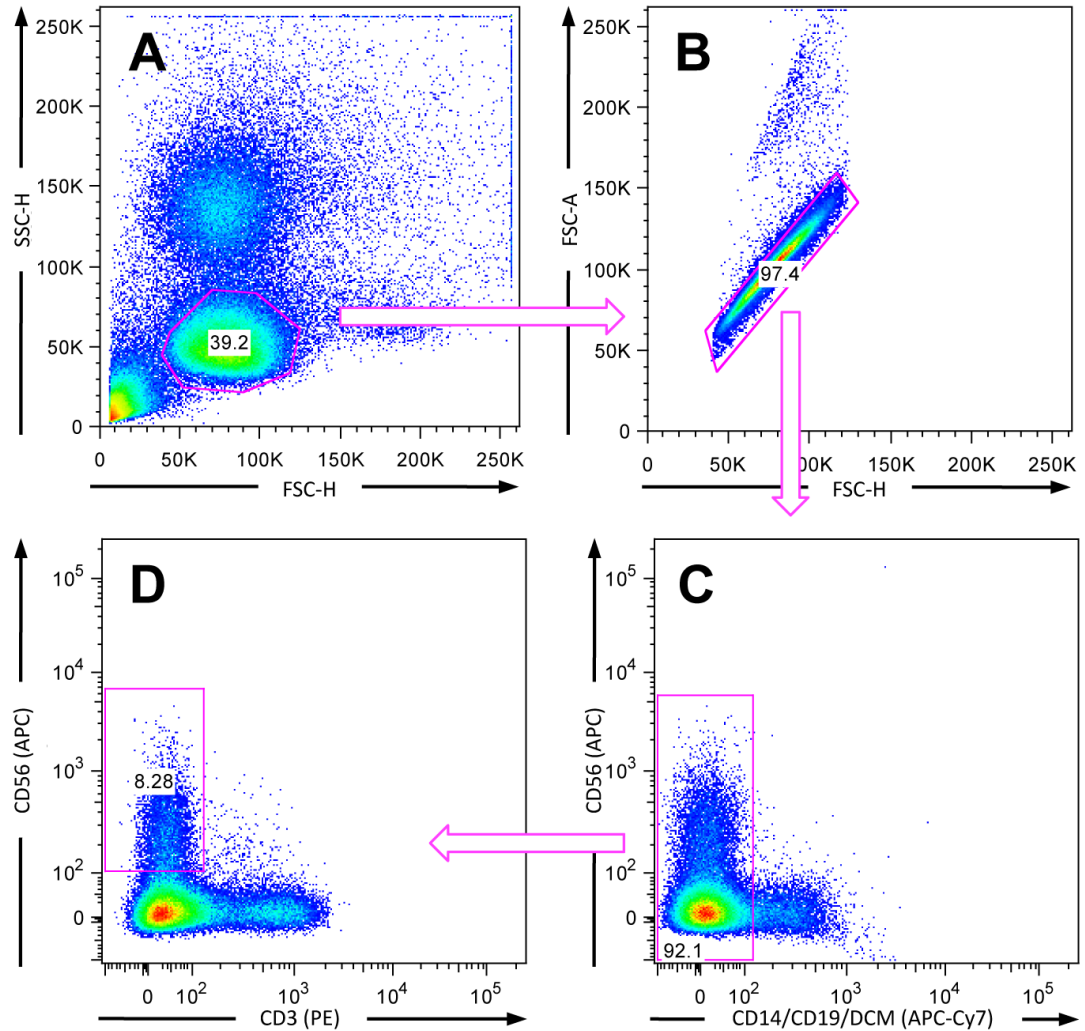


Figure 11 | Gating strategy to study effector functions of human CD3⁻CD56⁺ NK cells. NK cells were co-incubated with K562 target cells for 6h for assessment of cytokine production and 2 h for investigating degranulation at 37° C. After stimulation, cells were surface stained with fluorochrome-conjugated mAbs directed against CD3, CD14, CD19, CD56 and CD107a, as well as with DCM. The depicted gates were used to exclude (A) non-lymphocytes, (B) doublets, (C) CD14⁺/CD19⁺ and dead cells as well as (D) CD3⁺CD56⁻ cells from the analysis.

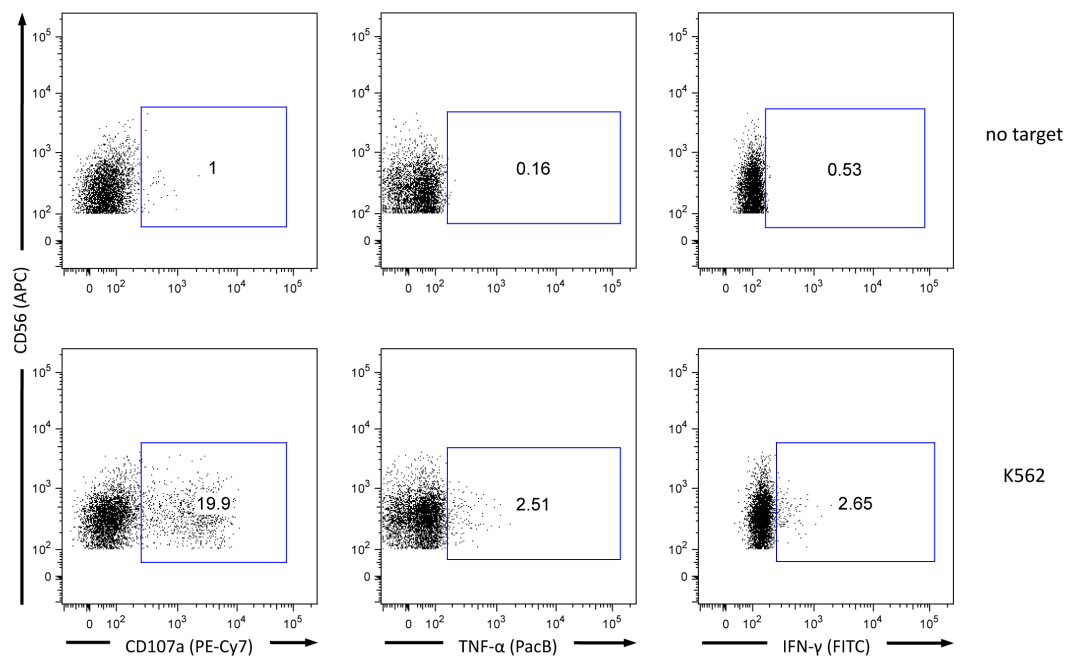


Figure 12 | NK cell cytokine production is induced by K562 target cells. PBMCs were incubated alone or activated with K562 target cells for six hours, fixed, permeabilized and stained with fluorochrome-conjugated mAbs. Profiles show CD107a surface expression and cytokine production of NK cells without activation and after co-cultivation with K562 target cells. Unactivated cells showed no significant responses (upper panel), incubation with target cells triggered degranulation and cytokine production (lower panel).

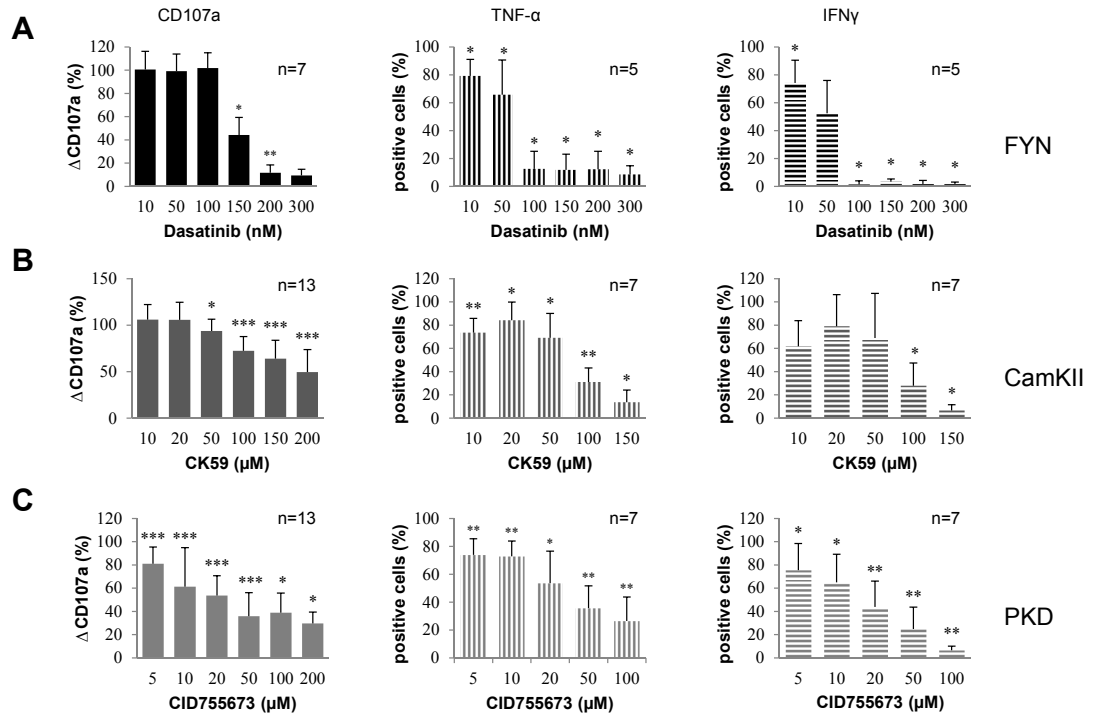


Figure 13 | Inhibition of Src family kinases, CaMKII and PKD decreases NK cell degranulation and cytokine release in primary human PBMCs. PBMCs were treated with [A] Dasatinib, directed against Src family kinases; [B] CK59, targeting CaMKII and [C] CID755673, inhibiting PKD-family kinases and subsequently incubated with K562 target cells at 37°C for 2 (degranulation) and 6 (cytokine release) hours, respectively. Cells were mixed with respective fluorochrome-conjugated mAbs and the frequency of degranulating or cytokine producing NK cells was determined via flow cytometry. Data represent values relative to corresponding DMSO control. Comparison of every inhibitor-treated group to its corresponding DMSO control group was performed by Wilcoxon test (* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$). Values represent mean of the indicated number of donors \pm SD.

3.2 MAIT cells isolated from human donor blood are suitable material for proteomic analyses

Compared to the effect that PKD inhibitor CID755673 had on NK cell activation in PBMC cultures, the effect on pure NK cell degranulation was moderate (Fig 14C). Application of the inhibitor only resulted in a small but still significant effect on CD107a⁺ cells. One donor showed a pronounced decrease at 200 μ M CID755673, while in two other donors a slight increase of degranulating cells could be detected at 50 μ M and 100 μ M. A different donor displayed a similar reaction at concentrations of 100 μ M and 200 μ M. In all donors, the accumulation of TNF- α was robustly inhibited at higher doses of CID755673. Two donors, however, showed a drastically pronounced TNF- α response at lower CID755673 concentrations, while a small increase of TNF- α ⁺ cells could be detected in another donor at 10 μ M CID755673. IFN- γ release was almost completely abrogated at concentrations of 100 μ M and higher. Again, at lower concentrations donor variations became obvious. Two donors showed a pronounced increase of IFN- γ positive cells to 270% and 200%, respectively, after initial reduction at lower concentrations. Two other donors also showed a small recovery of the IFN- γ response.

Overall, results obtained from purified NK cells were in accordance with results from PBMC cultures. Taken together, this data suggest that the respective kinases play an important role in NK cell activation and that tested kinase inhibitors could be used as drugs to modulate NK cell effector function. Furthermore, donor-dependent responses could be observed, that were pronounced in cultures of pure NK cells. Therefore, other cells might exert compensatory effect on NK cells in PBMC cultures.

3.2 MAIT cells isolated from human donor blood are suitable material for proteomic analyses

To gain material for proteomic studies, a pipeline for sample generation was established, and buffy coats generated from healthy human donor blood were obtained from the Blutbank Springe (Deutsches Rotes Kreuz; cooperation with H. Garritsen, Klinikum Braunschweig). Although MAIT cells are a predominant human T cell subset, especially in mucosal tissues and the liver, absolute numbers can be limited in peripheral blood that is the basis for buffy coats. For a systematic proteomic study it had to be verified that the provided blood samples would yield enough MAIT cells. As blood samples were provided as buffy coats and had not been screened for MAIT cell percentages before, it was also of interest if the MAIT cell amounts would differ from literature. Furthermore, only responsive, inactivated and not exhausted MAIT cells should be used for proteomics, so that the generated data would reflect the *in vivo* proteome of MAIT cells from healthy donors. Therefore, it had to be excluded that the cells are preactivated or exhausted, and cells had to be checked for viability.

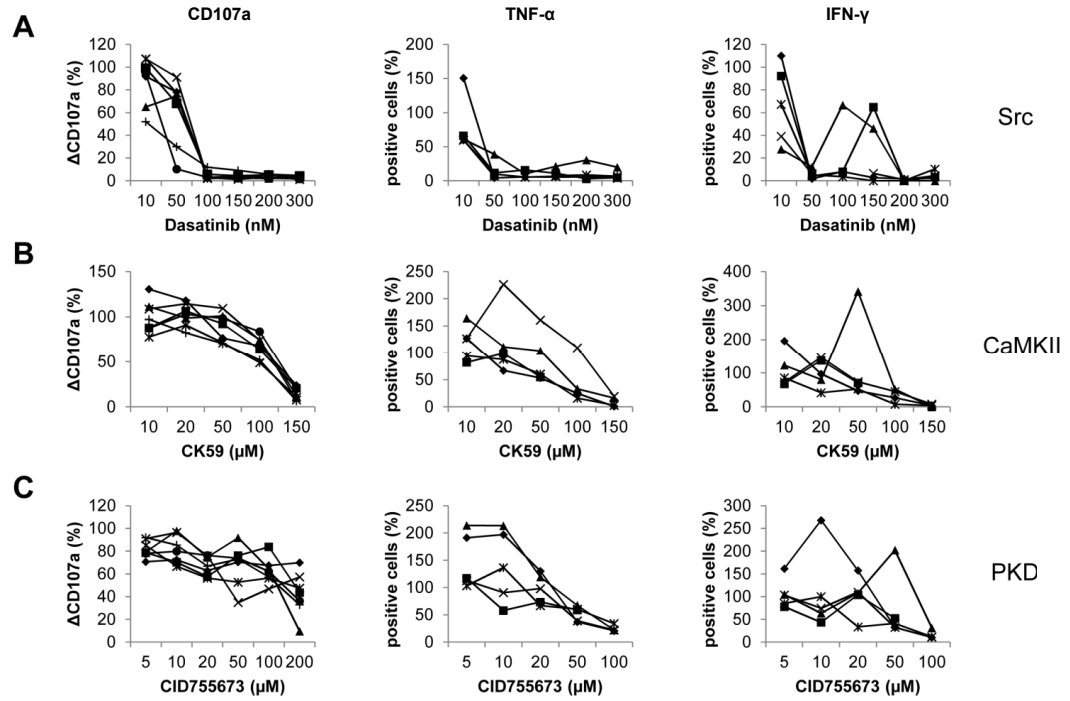


Figure 14 | Donor-specific responses of pure NK cells treated with Dasatinib, CK59 and CID755673. Purified NK cells were treated with [A] Dasatinib, directed against Src kinases; [B] CK59, targeting CaMKII and [C] CID755673, inhibiting PKD-family kinases and subsequently incubated with K562 target cells at 37°C for 2 (degranulation) and 6 (cytokine release) hours, respectively. Cells were mixed with respective fluorochrome-conjugated mAbs and the frequency of degranulating or cytokine producing NK cells was determined via flow cytometry. Data represents values relative to corresponding DMSO control. Comparison of every inhibitor-treated group to its corresponding DMSO control group was performed by Wilcoxon test (* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$). Values represent mean of the indicated number of donors \pm SD.

3.2 MAIT cells isolated from human donor blood are suitable material for proteomic analyses

Peripheral blood mononuclear cells (PBMCs) were isolated by density centrifugation from the blood of healthy human donors and stained with mAbs against CD3, V α 7.2 and CD161. The percentage of MAIT cells was then quantified by flow cytometry. To detect and quantify MAIT cells, lymphocytes were first gated on forward scatter (FSC)/sideward scatter (SSC) characteristics. Out of the lymphocyte populations, a gate was then set on T cells, that are defined by the expression of CD3 (TCR complex). In the T cell population, MAIT cells express the semi-invariant TCR chain V α 7.2 as well as high levels of CD161. The respective gating strategy is shown in Fig 15. Using this strategy, the percentage of MAIT cells in the T cell population was quantified in 20 different donors, in buffy coats obtained from the Deutsches Rotes Kreuz. In this study, MAIT cells made up from 0.1 % to 6 % of CD3-positive cells and showed a decline in numbers with increasing age (Fig. 16). Three donors had significantly higher numbers of MAIT cells than persons of the same age (age 25, 35 and 62, respectively). Interestingly, all these donors were male. Notably, data showed no significant deviations from current literature,^{137,138} although numbers were slightly lower in average. Additionally, a peak of MAIT numbers at roughly age 40 could not be detected, as no donors of this age were analyzed. Also, MAIT numbers are generally higher in women of reproductive age, which could not be detected in this donor set. In conclusion however, and with regard to the comparatively small sample size, the used method of MAIT isolation is suitable to isolate sufficient amounts of MAIT cells from donors healthy and inconspicuous human blood donors.

Additionally, it had to be assured that the isolated MAIT cells reflect their *in vivo* phenotype as close as possible, and are still functional and viable. To check for MAIT cell activity, *E. coli* were fixed with PFA and co-incubated with *ex vivo* PBMCs for 2 h, 4 h and over night, respectively, at different multiplicities of infection (MOI). This leads to presentation of bacterial ligands on MR-1 present on various cells in the PBMC culture, and subsequent activation of MAIT cells.¹²⁸ To enhance the stimulus, an antibody directed against the co-activatory receptor CD28 was added, while non-stimulated cells and cells co-incubated with anti-CD28 served as negative control. MAIT cell activation was then assessed by surface expression of activation markers CD69 and CD107a, that could be analyzed by flow cytometry (Fig. 17A, B). The MAIT cells in *ex vivo* PBMCs showed an increased surface expression of CD69 and CD107a after stimulation, resulting in up to 30% cells showing CD69 or CD107a on the surface. This indicates a strong activation, and full functionality of the present MAIT cells. Over time it became apparent, that CD107a is rather a marker for early activation (Fig. 17C), showing strong surface expression after 2 h and 4 h already. The expression of CD69 however peaked later, showing the highest number of positive cells after over night incubation. Both results are in accordance with literature, where CD107a and CD69 are markers for granule exocytosis and long term activation, respectively.⁹⁴ Also, co-incubation

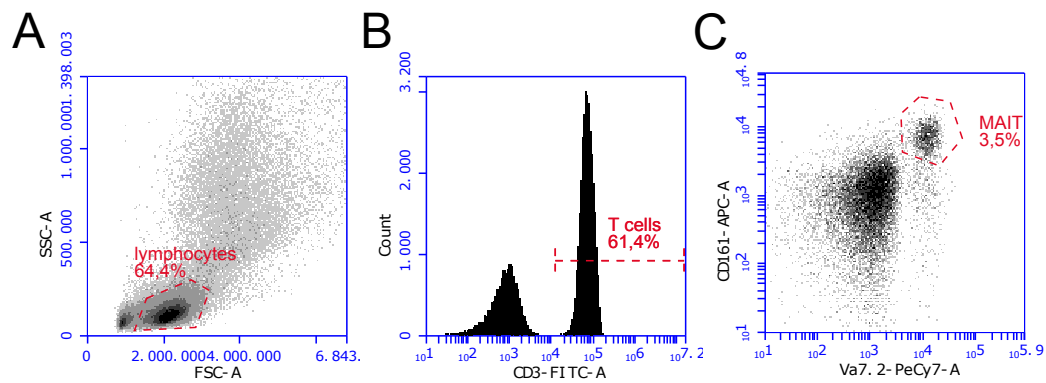


Figure 15 | Gating strategy for primary human MAIT cells. PBMCs were isolated from human donor blood, stained with mAbs and analyzed by flow cytometry. MAIT cells were gated as lymphocytes (A) that are positive for CD3 (B), and show expression of V α 7.2 as well as high expression of CD161 (C).

with the anti-CD28 antibody led to an increased response of both CD107a and CD69 surface expression. Additionally, triggering the cells with higher MOIs also increased the number of activated cells, showing that the cells can be activated dose-dependently and are not exhausted. Importantly, no preactivation through the culture medium, isolation protocol or other outside stimuli could be detected, as the negative controls showed no activated cells.

In summary, MAIT cells in *ex vivo* isolated PBMCs from healthy human donors can be activated to a great extent through co-incubation with stimulatory antibodies and fixed *E. coli* bacteria. Therefore, these MAIT cells are not pre-activated or exhausted and are suited well for representative proteomic analysis. Generated data will not be biased by *ex vivo* culturing, culture-based stimuli or effects from the sorting protocol, and be representative for prototypic MAIT cells.

3.3 First insights into the proteome of primary human MAIT cells reveal T cell specific proteins and pathways

Mucosal-associated invariant T cells (MAIT) cells are T cells, that display an effector memory phenotype, even without being primed by other immune cells or exposure to their antigen. Their phenotype is unique among T cells, but the proteome of MAIT cells has never been investigated before. Therefore, it was decided to conduct a pilot study to define the proteome of primary human MAIT cells, and get the first insight into their unique proteome.

One representative donors was selected and a strategy was established to sort MAIT cells from PBMC cultures (2.6.2). PBMCs were stained with monoclonal antibodies directed

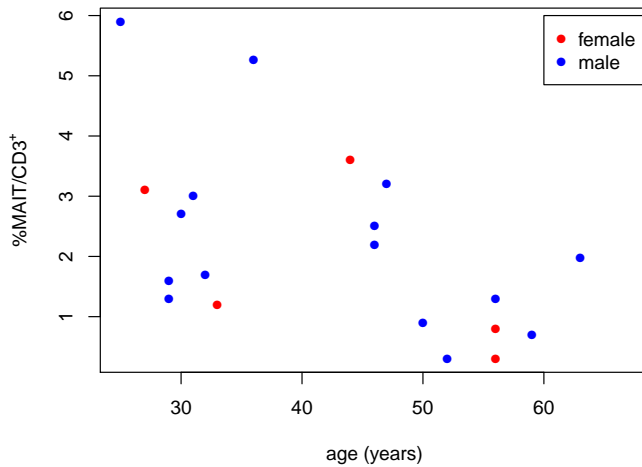


Figure 16 | Percentage of MAIT cells in various human donors. PBMCs were isolated from 20 human donors, and the amount of MAIT cells was quantified by flow cytometry. MAIT cell numbers decrease with age, and might have a small increase until a age of roughly 40 years. Three male donors show an increased number of MAIT cells, compared with persons their age (age 25, 35 and 62, respectively).

against CD3, CD161 and TCR chain $V\alpha 7.2$, and sorted by flow cytometry (2.6.3). The chosen separation strategy is shown in Fig 18. First, lymphocytes were gated due to their unique characteristics regarding size and granularity, which were assessed by their ability to scatter forward (FSC, forward scatter) and side light (SSC, side scatter), respectively. Doublets were excluded on the basis of the fact that such cell aggregates passing the detector show an disproportional high integrated area of signal intensity when compared with the height of signal intensity. This mismatch is detectable with both forward and side scatter light (FSC-A vs. FSC-H and SSC-A vs. SSC-H, respectively). After the exclusion of doublets, MAIT cells were then defined as CD3-positive cells, that express both CD161 in high amounts, as well as the invariant T-cell receptor chain $V\alpha 7.2$ ($CD3^+V\alpha 7.2^+CD161^{++}$). This strategy yielded a purity of 97 % MAIT cells, with $0.7 \cdot 10^6$ MAIT cells isolated in total. After sorting, cells were pelleted and lysed. Proteins were then digested with Trypsin (see 2.7.1), the generated peptides were cleaned up (see 2.7.2), and the proteome of MAIT cells was defined by LC-MS/MS (see 2.7.5) without prior sample subfractionation. In total, out of 120 795 spectra generated by the mass spectrometer, 9235 could be assigned to 3975 different peptides with a minimum peptide score of 30 (for complete search parameters see Tables 6 and 7). These data could be used to identify 1287 proteins.

Figure 19 shows a representative peptide spectrum. Peptide fragmentation in the mass spectrometer results in fragment ions that can, together with the knowledge of amino acid masses, be used to sequence the specific peptide. Mascot software (Matrix Science) then compares peptide sequence with a database of *in silico* generated tryptic peptides, that is generated from the Swiss-Port/UniProt database, and thereby identifies the peptides belonging

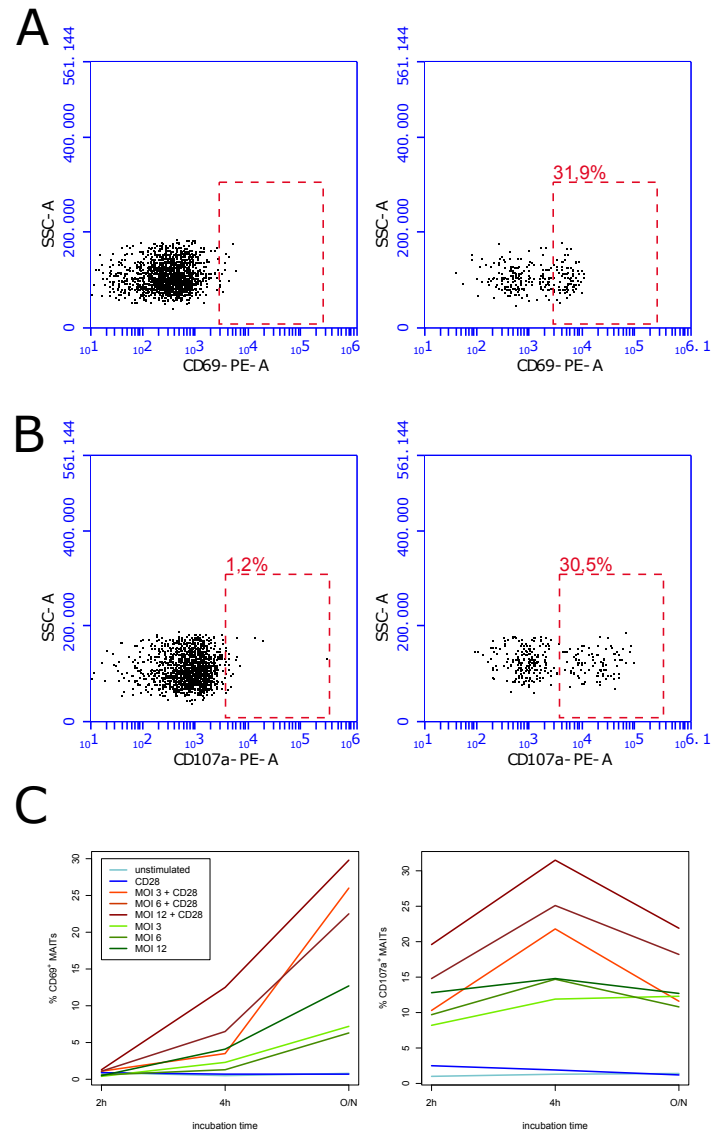


Figure 17 | Activation of primary human MAITs with *E. coli*. PBMCs were coincubated with different MOI of fixed *E. coli* and with or without the presence of anti-CD28 antibody. Surface expression of activation markers CD107a and CD69 was then analyzed by flow cytometry using different incubation times. (A) After over night incubation with fixed *E. coli* and antibody against CD28, upregulation of activation marker CD69 could be detected on MAIT cells. (B) Flow cytometry could detect a significant increase of CD107a-positive cells after four hours on incubation with fixed *E. coli* and CD28. (C) Also, a time-, CD28- and MOI-dependent increase of CD107a and CD69 surface expression could be detected. Figure shows one representative donor.

to the spectrum. Also, a score that allows to judge the reliability of the data is calculated (Mascot Peptide Score). With the peptide identified, it is also possible to determine the corresponding protein. Furthermore, a score for every protein can be calculated that also considers the number of different peptides that have been identified and assigned to this protein. In this study, no proteins were considered that showed a peptide score of below 30. Software ProteomeDiscoverer (Thermo Scientific) was then used to further analyze and visualize the data. A full list of search parameters and filters can be found in Tables 6 and 7. In this example, the peptide sequence ISALTALR was then assigned to a unique tryptic peptide of the pore-forming protein perforin, that is absolutely vital for the function of cytotoxic immune cells like MAIT cells.

Importantly, proteins with vital crucial immunological functions, like granzymes A and K could also be identified in MAIT cells (see Table 8). Also, T cell surface markers like CD8 or CD44, or the degranulation marker lysosome-associated membrane glycoprotein 1 (LAMP-1, CD107a) could be identified. This shows that not only access to important, but rather low abundant proteins is possible with LC-MS/MS, but also surface proteins can be identified. To gain an overview about MAIT cell proteins, identified proteins were annotated in Proteome Discoverer with Gene Ontology terms (GO terms) regarding their localization (GO cellular component). This annotation of localization (see Fig. 20) showed the majority of identified proteins to be cytoplasmic (34 %), which other large proportions being located at the membrane (18 %), in the nucleus (17 %) or in the mitochondria (6 %). Smaller percentages were identified to be localized in various compartments. This indicates that proteins of the major compartments of MAIT cells could be isolated and identified with the used protocol, and the localization of identified proteins also roughly resembles the distribution of proteins observed in human cells before.¹³⁹ To check if relevant immunological pathways could also be covered in this analysis, the list of identified proteins was annotated to Gene Ontology biological processes with the help of the Database for Annotation, Visualization and Integrated Discovery (DAVID).^{140,141} Data revealed that 13 T cell specific processes were covered in this first snapshot of the MAIT cell proteome (see Table 9), with a minimum of three proteins identified per process. This shows that the proteomic approach is also suitable to analyze abundance of proteins and pathways that are relevant for differentiation or activation of T cells.

Taken together, first analysis of the MAIT cell proteome showed that the used experimental procedure allows access to proteins from several cellular compartments, with the distribution of proteins being in accordance with literature. Even low-abundant proteins with immunological functions could be identified. Also, data indicated the presence of different T cell specific pathways in this first pilot experiment. Although, the presence of these pathways

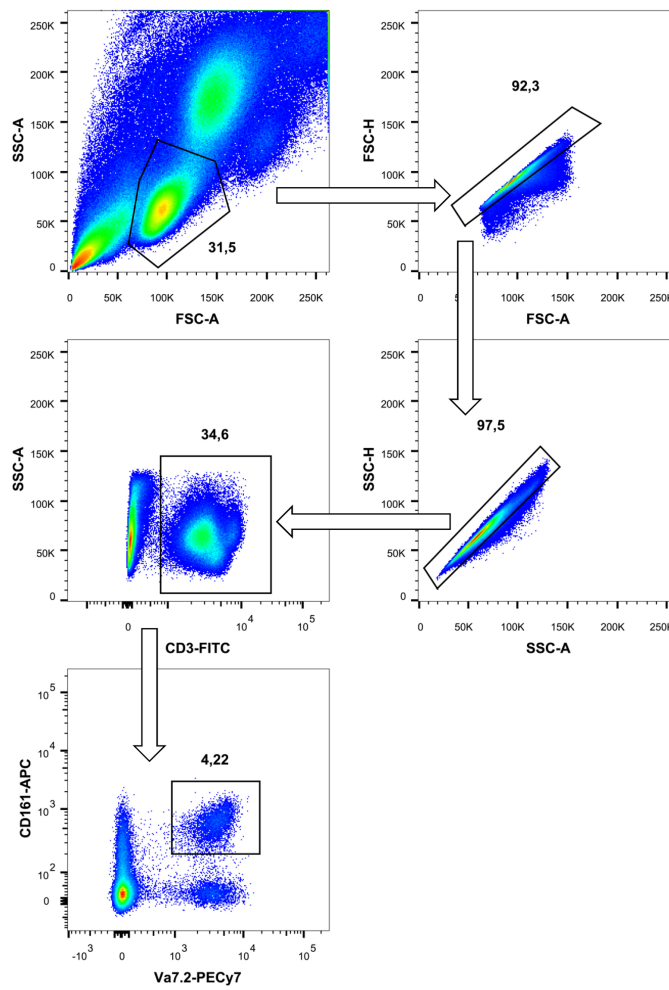


Figure 18 | Gating strategy for the isolation of primary human MAIT cells via FACS. PBMCs were isolated from the blood of a human donor, stained with antibodies specific for CD3, CD161 and V α 7.2, and sorted by FACS. MAIT cells were defined as lymphocytes (A), that are not doublets (B and C), express CD3⁺ (D), and are not positive for V α 7.2 but also show a high expression of CD161 (V α 7.2⁺CD161⁺⁺, E).

suggest a T cell phenotype for MAIT cells, the picture of the MAIT cell proteome is still very fragmentary. To be able to identify unique mechanisms, MAIT cells have to be compared with prototypic innate and adaptive immune subsets. This will also allow to assess similarities and differences between the cell types. Furthermore, it is necessary to increase the resolution of the mass spectrometric analysis by prior subfractionation, and gain access to a higher number of proteins even.

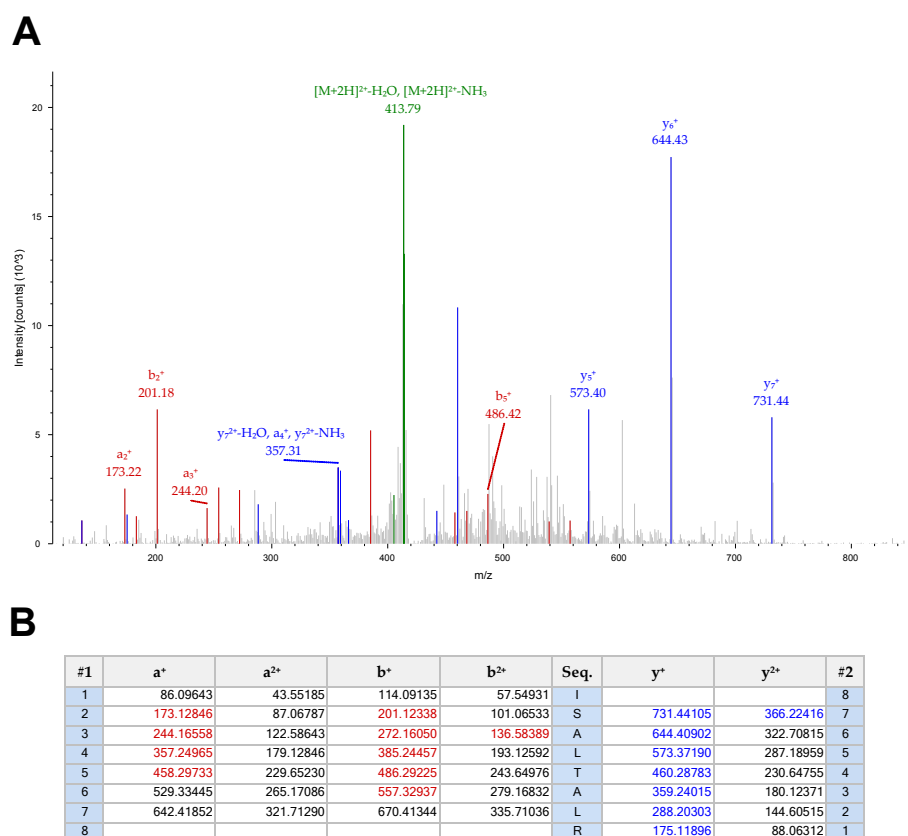


Figure 19 | MS/MS spectrum of cytolitic perforin peptide ISALTALR. The proteins of MAIT cells were digested with trypsin and the peptides analyzed by mass spectrometry. In the mass spectrometer, peptides were fragmented and b- and y-ions generated (red and blue, respectively). Peptide sequence ISALTALR could be derived from these ions through defined amino acid masses. The sequence was then assigned to a unique peptide of the pore-forming protein perforin from the Swiss-Prot/UniProt database, with using the search parameters and filters displayed in Tables 6 and 7. (A) shows the detected peptide spectrum and (B) the assigned masses of the ions, from which the mass differences can be used to define the amino acid sequence. Assigned mascot score for this peptide was 31.

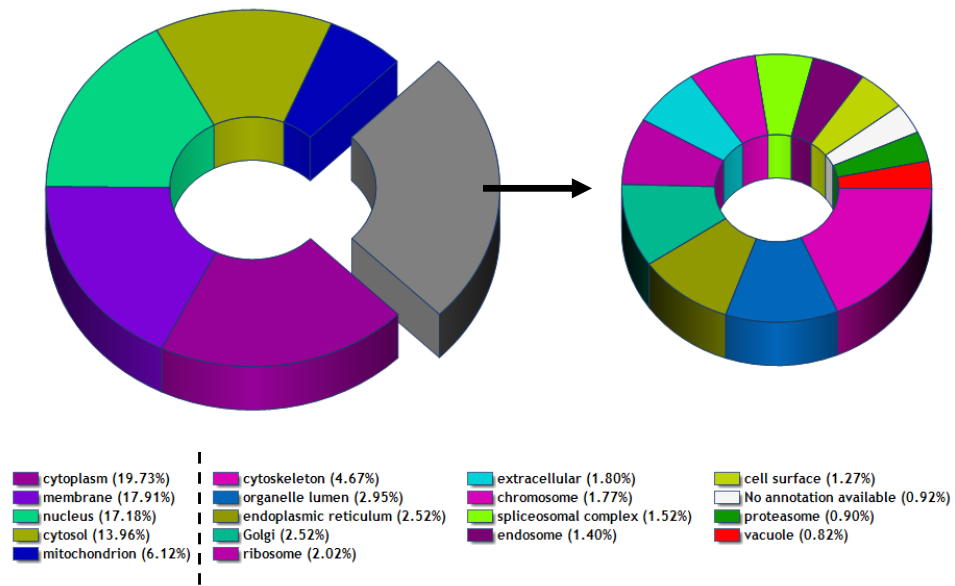


Figure 20 | Localization of proteins identified in a proteomic analysis of MAIT cells. The proteome of isolated MAIT cells was defined by mass spectrometry and the proteins were annotated regarding their subcellular location with the help of GO terms. The five highest abundances are displayed on the left side. The gray chunk contains a high variety of lower abundant localizations, and is displayed in detail on the right side. The largest proportions of annotated proteins are localized in the cytoplasm, membrane and nucleus, respectively.

Table 8 | Selected proteins with immunological function identified in MAIT cells

Name	Mascot score	Coverage	Unique peptides	Unique spectra
CD8 alpha chain	78.98	7.66 %	1	2
CD5	29.82	2.24 %	1	1
CD48	59.29	5.76 %	1	2
Lysosome-associated membrane glycoprotein 1	50.94	5.04 %	1	1
Granzyme A	251.38	19.08 %	5	9
Perforin-1	31.12	1.44 %	1	1
CD44	289.32	6.33 %	4	11
Granzyme K	441.84	31.82 %	5	11

Table 9 | Pilot study of the MAIT proteome indicates the presence of T cell specific pathways

GO Term Name	Count	Proteins (UniProt Accession)
positive regulation of alpha-beta T cell activation	7	P00491; P43403; P08575; O00203; Q8WWP7; O75995; P00813
positive regulation of alpha-beta T cell differentiation	6	P00491; P43403; O00203; Q8WWP7; O75995; P00813
negative thymic T cell selection	4	P16150; Q92608; P43403; P08575
negative T cell selection	4	P16150; Q92608; P43403; P08575
positive regulation of T cell differentiation	7	P00491; P43403; P08575; O00203; Q8WWP7; O75995; P00813
positive regulation of T cell activation	12	P16150; P31146; P06239; P00491; P43403; P10809; P08575; O00203; Q8WWP7; P06127; O75995; P00813
regulation of alpha-beta T cell differentiation	6	P00491; P43403; O00203; Q8WWP7; O75995; P00813
T cell proliferation	6	Q92608; Q07812; P08575; P62942; P06241; P32119
negative regulation of T cell mediated immunity	3	P16150; P08575; P16298
thymic T cell selection	4	P16150; Q92608; P43403; P08575
T cell differentiation	10	P01732; P16150; Q92608; P06239; P43403; P08575; P35268; Q8WWP7; P78527; P16298
T cell activation	23	P16150; Q92608; P01732; P06239; P42768; P08575; P35268; P39656; P62942; P09326; P35579; P78527; P16298; P27487; P10809; Q07812; P43403; P20701; Q8WWP7; P06241; P13796; P32119; P00813
regulation of T cell mediated immunity	7	P16150; P61769; P27487; P10809; P08575; O75995; P16298

3.4 Mass spectrometry generates highly reproducible data from small cell numbers

The increasing sensitivity of modern mass spectrometers has also lowered the amount of sample material required for a proteomic analysis of complex samples. With newest techniques, data can be generated from cell numbers as small as 1 000 HeLa cells.¹⁴² However, when working with primary material, usually higher cell numbers are required, due to the comparatively low protein amount in primary cells. Ideally, proteomics is done with at least 500 000 or 1 000 000 primary cells. The cell number of MAIT cells in buffy coats however can be limited to a magnitude as small as 250 000 MAIT cells per buffy coat, or even lower. Thus, a proteomic workflow had to be established that allowed lysis, digestion, labeling, clean-up and subfractionation of samples while minimizing the loss of material during the process, while at the same time providing high reproducibility. Also, it had to be tested if subfractionating these small amounts of proteins would actually increase the sensitivity of the mass spectrometer and the number of identified proteins, in comparison with not-fractionated samples as in 3.3. Therefore, the proteome of 250 000 primary PBMCs was to be analyzed by mass spectrometry, after SCX subfractionation. Another aspect the used protocol had to be checked on was consistency over several experiments. Two factors generally influence the reproducibility between experiments. First, donor variations increase the variance in different samples, but allow the identification of important, donor-independently regulated proteins. More importantly, the analytical pipeline might also lead to different results, even when the same experiments are repeated.

After isolation of PBMCs from human donor blood (see 2.6.2), 250 000 cells were lysed with urea (see 2.7.1). The urea based lysis therefore is a protocol which minimizes samples loss through a minimum of washing or purification steps. However, this might result in a not completely purified protein mixture, containing contamination with e.g. membrane fragments. After lysis, cells were digested with trypsin, desalted (see 2.7.1 and 2.7.2) and subfractionated into 40 fractions by SCX chromatography (see 2.7.4). The chromatogram of the SCX fraction shows the elution of the peptides after increasing the concentration of the high salt elution buffer, with a peak of eluting peptides from fractions 13 - 24 (Fig. 21).

First, the SCX fractions 13 to 24, that contain the vast majority of the peptides, were desalted again (see 2.7.1) and analyzed by mass spectrometry as described (see 2.7.5), but with a short 60 minute gradient on the upstream LC separation unit. Sixty minutes were chosen due to the small amount of peptides present in the sample. In this analysis, 2260 proteins could be identified out of 227 000 spectra, that had resulted in the sequencing of 8198 peptides. This shows that subfractionating the sample, as expected, increases the

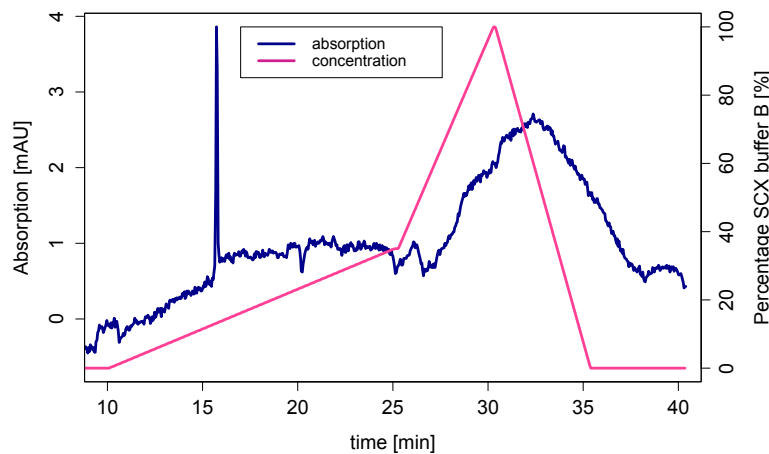


Figure 21 | Chromatogram of SCX subfractionation of 250 000 cells. Tryptic peptides were loaded onto a Mono-S-PC1.6/5-column and eluted by increasing concentration of the high salt elution buffer (violet). As every minute a new fraction was collected, the time corresponds with the number of the fraction. The amount of eluted peptide correlates with the absorption of UV light at 214 nm (blue). Fractions collected at time points 13 - 24 show the most absorption, the peak at minute 34 is most likely a contamination. Due to the small amount of peptides in the sample, the peaks are comparatively small. Fractions 13 - 24 were therefore chosen for further analysis.

sensitivity of detection. Only 1200 proteins could be identified out of 10^6 cells used in 3.3, without prior subfractionation, while the peptides of only 250 000 cells resulted in 2260 identified proteins. Also, identified proteins were again annotated regarding their subcellular localization. Gene Ontology revealed a similar distribution as observed before (see 3.3), with 32 % of the proteins localized in the cytoplasm, 20 % at the membrane, 15 % in the nucleus and 5 % in the mitochondria. Again, small percentages of proteins were also annotated to smaller compartments like the endosome.

To investigate if the experimental set-up leads to reproducible results and the variation that is caused by sample processing is minimal, a tryptic digest of 500 000 cells from one donor was split into two samples, differentially labeled with isobaric iTRAQ tags (see 2.7.3), and mixed again. iTRAQ labels allow relative quantification of peptides in the mass spectrometer and a quantitative comparison of the samples.¹⁴³ Through their peptide reactive group, these isobaric tags are chemically linked to every peptide present in the sample mixture. Every tag also contains a reporter and a balancer group, all these groups having a defined mass. Upon fragmentation in the collision cell, the reporter and the balancer dissociate from the labeled peptide, and the former can be detected by the mass spectrometer (Fig. 23). By comparing the intensity of the reporter signals, a relative regulation factor for the

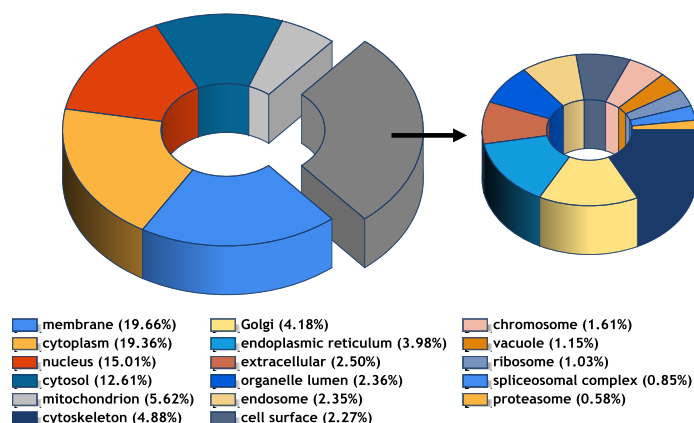


Figure 22 | Localization of proteins identified in a proteomic analysis of primary human PBMCs. The proteome of 250 000 PBMCs was defined by mass spectrometry and the proteins were annotated regarding their subcellular location with the help of GO terms. The five highest abundances are displayed on the left side. The gray chunk contains a high variety of lower abundant localizations, and is displayed in detail on the right side. The largest proportions of annotated proteins are localized in the cytoplasm, membrane and nucleus, respectively.

peptide and the corresponding proteins can be calculated. Importantly, the analysis software Proteome Discoverer also applies a median-based normalization algorithm before comparing the intensities. This algorithm normalizes all peptide ratios for each channel by the median peptide ratio. In this experiments, labels with reporter ions of the mass 114 Da and 115 Da were used, all \log_2 RF display the relation of the intensity of the reporter 115 to the intensity of the reporter 114. Also, regulation factors (RF) are displayed as logarithm to base 2. A \log_2 RF of 0 therefore indicates no difference between the two compared reporters, while \log_2 RF 1 would mean a two-fold increased intensity of 115 compared to 114. After the labeling process, samples were desalted, mixed, subfractionated, desalted again and analyzed by mass spectrometry as described before in this chapter.

No donor variation of protein abundance should be detectable, as both samples came from the same donor. Every visible variation had therefor its basis in the analytical pipeline. Evaluation of the relative iTRAQ signals and calculation of the regulation factors indeed indicated a high reproducibility of the experimental set-up (Fig. 24). As expected, most of the identified proteins didn't show variation of abundance between the identically treated 114 and 115 samples. Ninety percent of the identified proteins showed \log_2 RF between -0.27 and 0.34, with minimal and maximal values of -1.18 and 2.96, respectively. Additionally, only six proteins were annotated with a two-fold increase or decrease in the 115-labeled sample. The more robust a protein was identified, the higher was the probability of it not being identified

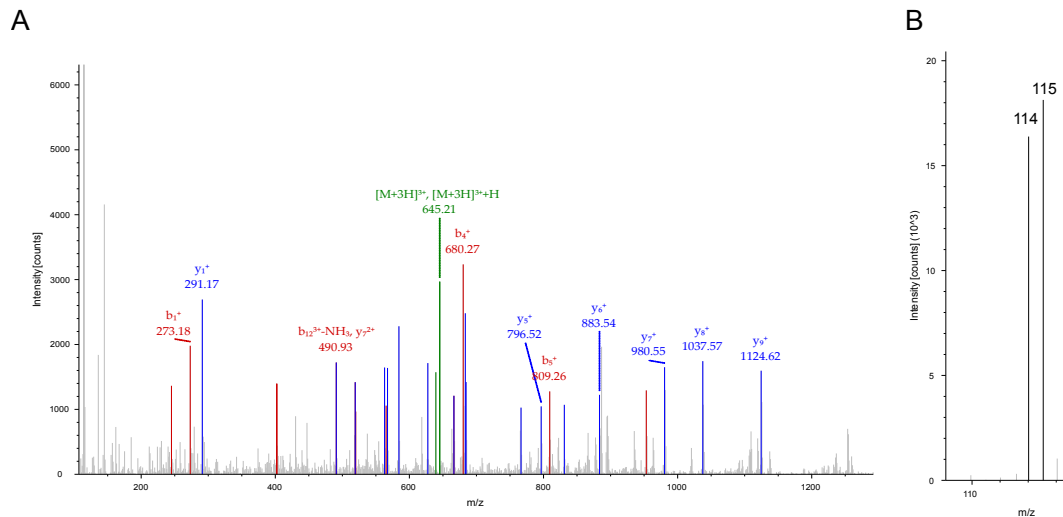


Figure 23 | MS/MS spectrum of an iTRAQ-labeled peptide of actin. PBMC proteins were digested with trypsin, labeled with iTRAQ reagent and the labeled peptides analyzed by mass spectrometry. (A) In the mass spectrometer, peptides were fragmented and b- and y-ions generated (red and blue, respectively). Peptide sequence QEYDESGPSIVHRK could be derived from these ions through defined amino acid masses, and was assigned to actin, which is an important component of the cytoskeleton. Also, iTRAQ reporter ions with the masses 114 and 115, respectively, were detected. (B) The relative intensity of the reporter ions, as seen enlarged on the right side, can be used to comparatively quantify the amount of actin present in the sample. The amount of actin in both samples is equal, the calculated regulation factor (RF) 115/114 for this peptide after normalization is 0.959, resulting in a \log_2 RF of -0.06. The calculated \log_2 RF for actin in the sample is -0.03.

as regulated. This indicates that the proteins that were found with a pronounced difference of abundance between the identical samples might be an artifact of erroneous quantification.

First, data indicated that the used protocol was suited to generate sufficient amount of data even from small numbers of primary cells. Although only 250 000 cells were analyzed, subfractionation allowed identification of 2260 proteins. Also, results illustrated the high reproducibility of the used experimental procedure. However, artifacts that were found to be differently expressed in the identical samples underlined the need for a bigger sample size in following experiments. Also, a statistical model was needed that helps to identify and remove these variations, and identify proteins that are consistently regulated in every experiment. Taken together, a protocol was established, tested and improved step by step, that allows the reproducible proteomic analysis of small numbers of primary human blood cells. With this protocol it will now be possible to comparatively analyze the proteome of MAIT, NK and conventional CD8+ T cells.

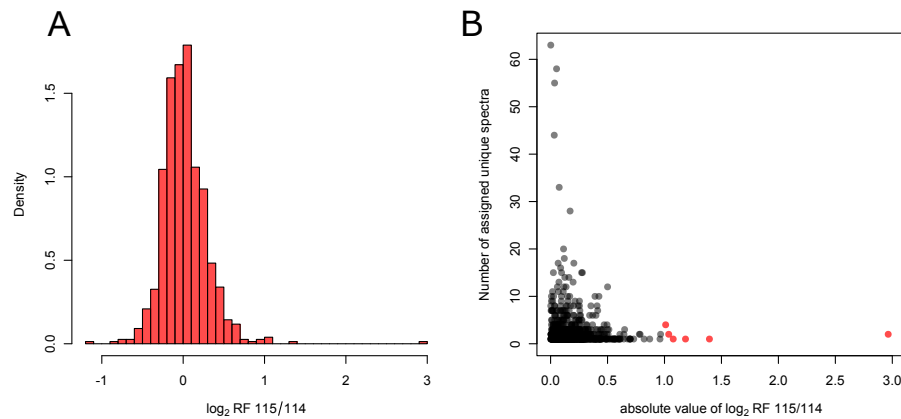


Figure 24 | Technical replicates of MS samples show high reproducibility. Two samples of PBMCs of the same donor were labeled with different iTRAQ labels, and analyzed by mass spectrometry (MS). (A) Most of the identified proteins show no different abundance between the two identical samples. Ninety percent were quantified with a \log_2 RF between -0.27 and 0.34. (B) Proteins that showed an at least two-fold change of abundance between both samples (red) were identified with a low number of unique spectra.

3.5 Conserved and novel functions in innate immunity in MAIT cells

3.5.1 Flow cytometry allows the generation of highly pure MAIT cells, CD8⁺ T cell and NK cell samples

MAIT cells are a recently discovered T cell subset that is highly abundant in human peripheral blood, mucosal tissues and displays innate properties. Conventional CD8⁺ (cCD8⁺) T and NK cells are major subsets of adaptive and innate immunity that are functionally well defined. In MAIT cells, mechanisms that are crucial for their innate phenotype are not well defined yet, but can be revealed by comparative proteomic analyses. For a reproducible proteomic study, not only a reproducible, sensitive protocol is necessary, that had been established already in the course of this thesis (3.4). Also sample generation, that in this case was supported by fluorescence-activated cell sorting, had to be standardized and reproducible. Purity of cell types needed to be as high as possible, to avoid contamination, while also enough material for proteomics had to be isolated.

First, an flow cytometric isolation strategy for all these immune cells had to be devised. PBMCs were isolated from human donor blood of five donors (2.6.2), stained with monoclonal antibodies directed against CD3, CD8, CD56, CD161 and V α 7.2, and sorted by flow cytometry (see 2.6.3). The chosen separation strategy is shown in Figure 25A. First, lymphocytes were gated due to their unique characteristics regarding size and granularity, which were assessed

by their ability to scatter forward (FSC, forward scatter) and side light (SSC, side scatter), respectively. Doublets were excluded as before (FSC-A vs FSC-H and SSC-A vs. SSC-H, respectively; 3.3). After the exclusion of doublets, NK cells were defined as CD3-negative cells that express CD56 (CD3⁻CD56⁺). MAIT cells were sorted and were defined as CD3-positive cells, that express both CD161 in high amounts, as well as the invariant T-cell receptor chain V α 7.2 (CD3⁺V α 7.2⁺CD161⁺⁺). Additionally, conventional CD8-positive T cells (cCD8⁺) were sorted for analysis. As a significant amount of MAIT cells also expresses CD8, cCD8⁺ T cells for this study were defined as CD3⁺CD8⁺ single cells that are not MAIT cells. Details about each sorting experiment are shown in Table 10. Purity was assessed when already sorted cells were analyzed again by flow cytometry, and defined as percentage of the respective cell subset compared to the number of total detected events. In most cases, purity of 90 % or higher could be achieved. However, purified NK cells in general showed a lower purity. This phenomenon is an fluorochrome effect. Along the sorting process that can take up more than six hours, CD56-PE/Cy5 signal gets dimmer over time as the fluorochrome degenerates and becomes less intensive. This lead to a larger number of cells not fitting into the CD56⁺ gate anymore at the purity check after sorting is completed (Fig. 25B), and to misprizing of the purity. Most importantly, no contamination by other cell types could be observed in the NK cells fraction. Also, no increased amount of dead cells or debris was detected. Therefor, the low purity is definitely a result of fluorochrome degradation underscoring, and far higher than displayed.

NK cells and CD8⁺ T cells are higher abundant than MAIT cells, meaning that the number of MAIT cells would restrict the number of used cells in every experiment. Thus, donors were pre-screened and only donors with higher amounts of MAIT cells were selected for sorting. Although MAIT cell numbers still varied significantly, at least 10⁶ MAIT cells could be collected for every donor (Tab. 10). Absolute numbers of NK and cCD8⁺ T cells are much higher and collection of these high abundant cell types was stopped after collecting a certain number. Percentages of MAIT cells varied between 2 - 5 % of their parent CD3⁺ cell population. Percentages of NK cells and cCD8⁺ T were significantly higher, varying between 9 - 27 % and 23 - 35 %, respectively.

In summary, buffy coats provide enough material of the established sorting protocol allowed the standardized sample generation of defined cCD8⁺, NK and MAIT cell populations. Isolated cell populations are highly pure and also provide sufficient material for comparative MS analysis.

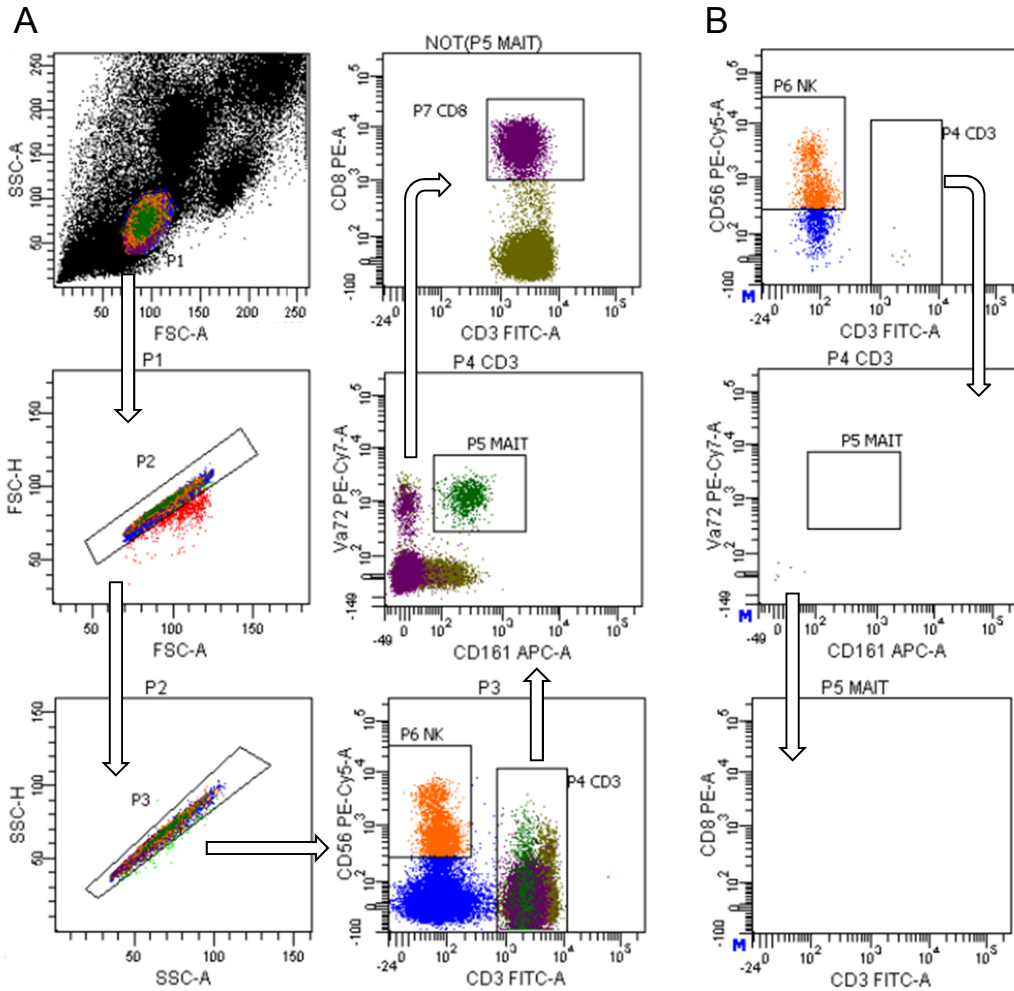


Figure 25 | Isolation of primary human MAIT, NK and CD8⁺ T cells from PBMC cultures. PBMCs were isolated from human donor blood, stained with antibodies specific for CD3, CD8, CD56, CD161 and V α 7.2, and sorted by FACS. (A) NK cells were defined as single cells that are CD56-positive and not T cells (CD3⁻CD56⁺), MAIT cells as single T cells (CD3⁺) that are positive for V α 7.2 and show a high expression of CD161 (V α 7.2⁺CD161⁺⁺) and conventional CD8⁺ T cells as single T cells that express CD8 and are not MAIT cells (non-MAIT CD3⁺CD8⁺). (B) After sorting, cells were checked for purity by flow cytometry. NK cells show a loss of CD56 signal. However, no contamination with other cell types could be observed.

Table 10 | Donor information, purity and cell number of sorted MAIT, NK and cCD8⁺ T cells

donor information			purity [%]			cell number [$\cdot 10^6$ cells]			percentage of parent population [%]		
donor	age	sex	MAIT	NK*	cCD8 ⁺	MAIT	NK	cCD8 ⁺	MAIT	NK	cCD8 ⁺
1	44	f	90.4	57.5	91.5	3.4	12.0	10.0	3.9	27.0	31.9
2	36	m	92.9	80.2	91.5	9.78	13.5	13.5	5.3	24.1	22.8
3	46	m	92.5	87.3	94.1	1.7	4.5	4.5	2.13	15.0	22.7
4	27	f	93.6	58.6	91.6	4.1	4.5	4.5	2.8	8.9	30.2
5	25	m	93.9	57.7	85.4	2.3	4.5	4.5	5.3	12.7	35.0

*Purity of NK cells is displayed lower than the actual due to degradation of the CD56-PE/Cy7 fluorochrome over the course of the sorting process.

3.5.2 Protein identification in MAIT, NK and cCD8⁺ T cells shows large overlap of proteins in different donors

After generation of highly pure immune cell samples of MAIT, NK and cCD8⁺ cells, the established proteomic workflow could be executed to generate highly accurate quantitative proteomic data. The proteome can be defined for every donor and the overlapping proteome of all five donors can be identified. Also, data will allow first glimpses on the coverage of immunological pathways.

After isolation, cells were lysed with urea, peptides were digested (both 2.7.1) and each population (MAIT, NK, cCD8⁺) were labeled with isobaric tags (2.7.3). Labeling efficiency was checked for every donor and every channel with a 30 minute LC-MS/MS run, injecting 2 % of the sample. Proteome Discoverer was then used to quantify the percentage of labeled peptides areas of total peptide area. If label efficiency was below 95 %, samples were relabeled, desalted and checked again. The same mass spectrometric analysis was then used to quantify the peptide amount in every sample and channel, by calculating the total area of all precursor peptides. According to these data, for every donor samples were mixed with the same amount of labeled material for every channel and submitted to SCX chromatography (2.7.4). A representative chromatogram is shown in Figure 26, indicating that the most peptides were eluted in the fractions 15 - 25. Fractions 1 - 13, 27 - 34 and 34 - 38 were therefore pooled before desalting, and samples 14 - 26 were processed individually, resulting in 17 samples for every donor that were prepared for MS analysis (2.7.2). Samples were then analyzed with an Orbitrap Fusion mass spectrometer and spectra annotated to peptides and proteins with the help of Mascot and ProteomeDiscoverer software (2.7.5).

About 4000 proteins could be identified for every donor (Tab. 11). In total, 5636 different proteins could be annotated (see appendix for a complete list), with 2600 proteins being commonly identified in all five donors (Fig. 27). These 2600 proteins are high abundant in

Table 11 | Number of identified proteins per donor

	donor				
	1	2	3	4	5
assigned spectra	40196	39753	46227	65056	54496
identified peptides	16655	15997	17863	23803	19559
identified proteins	3887	3690	3865	4256	3981

every donor and cell type, and are expressed donor independently. Additionally, a number of 3323 proteins could be identified in at least four experiments, 3990 in at least three and 4653 in at least two experiments. All the identified proteins were functionally annotated with Pathway Studio for systematical analysis. Out of the total number of roughly 5600 proteins, analysis and annotation revealed association of 480 proteins to 38 immunological pathways. The relevance of the enriched pathways can be visualized by the calculation of a *p*-value, that represents significance, and the coverage of the specific pathway by the identified and annotated proteins. Not only the enriched immunological pathways with the highest percentage of annotated proteins, and therefor the highest *p*-values, can be mostly considered as NK or T cell specific (Fig. 28). Out of all 38 enriched pathways, 22 were exclusive for NK and T cell specific functions that could be detected with high coverage. Other covered pathways referred to general immunological processes like antigen presentation or cell death mediation.

In summary, the established workflow allowed the detection of 5636 proteins, with roughly 50 % of these proteins being detected in all five donors. These data indicate little donor variation regarding the presence of proteins, and underline the reliability of the data for further investigation. Also, this core proteome of roughly 2600 proteins contains the major components of the MAIT, NK and cCD8⁺ cell proteome. Accordingly, first functional annotation analysis showed a high coverage of immunological pathways. Specifically, pathways that are related to T and NK cell activity could be annotated, showing the presence and accessibility of proteins vital for immunological processes.

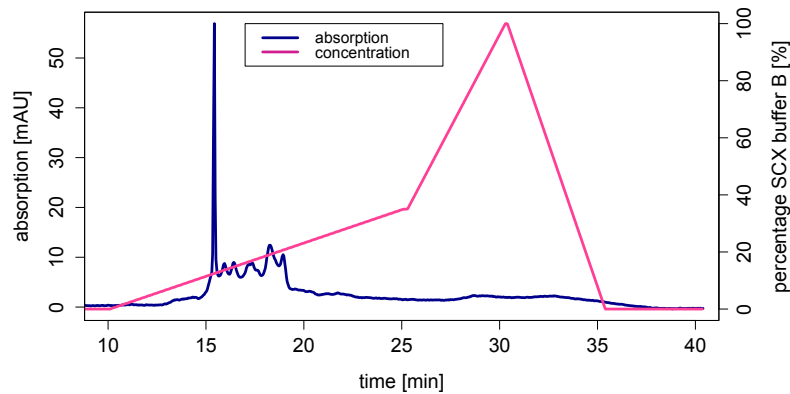


Figure 26 | SCX subfractionation chromatogram shows presence of peptide in different fractions. After lysis, MAIT, NK and cCD8⁺ cells were digested and labeled with different iTRAQ reagents. To increase sensitivity of mass spectrometry analysis, labeled peptides were mixed to the same amount, loaded onto a Mono-S-PC1.6/5-column and eluted by increasing concentration of the high salt elution buffer (violet). As every minute a new fraction was collected, the time in minutes is equal to the number of the fraction. The amount of eluted peptide correlates with the absorption of UV light at 214 nm (blue). Fractions collected at time points 15 - 25 show the most absorption, and therefore the highest amounts of tryptic peptides. These samples were processed individually while fractions 1 - 13, 27 - 34 and 34 - 38 were pooled.

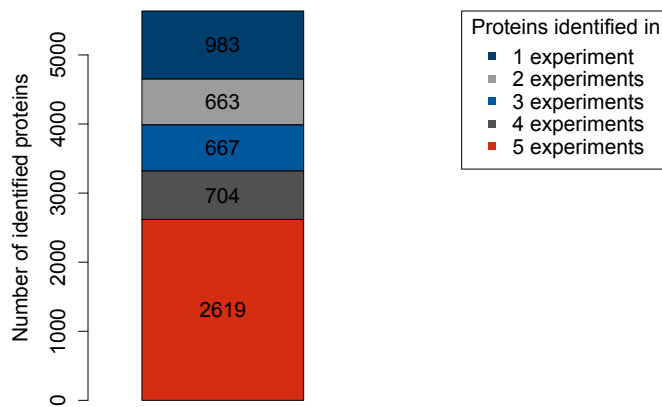


Figure 27 | Number of identified proteins in MAIT, NK and cCD8⁺ cells from five human donors. Human MAIT, NK and cCD8⁺ cells were isolated from blood of five different healthy donors. In total, 5636 proteins were identified. A number of 2619 proteins could be found in all five samples, while 3323 proteins could be identified in at least four, 3990 in at least three and 4653 in at least two experiments.

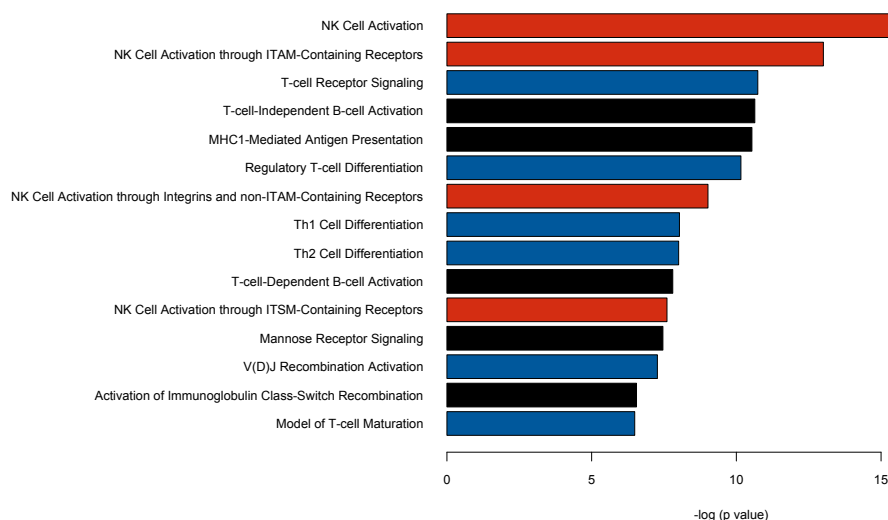


Figure 28 | Pathway annotation of all identified proteins in MAIT, NK and cCD8⁺ cells The proteome of isolated human MAIT, NK and cCD8⁺ cells was defined by mass spectrometry. Identified proteins were annotated to immunological pathways with Pathway Studio, with the coverage of the pathways calculated as *p*-value, here shown as negative logarithm. Among the fifteen highest enriched pathways, ten are directly associated with NK and T cell activity (red and blue, respectively).

3.5.3 Differential protein expression in MAIT, NK and cCD8⁺ T cells

3.5.3.1 MAITs cells are a cell type distinct from NK and cCD8⁺ T cells on the proteomic level

Additional to protein identification, MS analysis also permits relative quantification of iTRAQ labeled peptides. This allows the calculation of regulation factors for single proteins, and these can be used to estimate the difference of the cell types on the proteomic level. Furthermore, when comparing regulation factors for the same proteins between donors, donor variation on the level of protein abundance can already be estimated.

Only proteins that were identified in all five donors were used for this analysis. Figure 29 shows a representative spectrum of this analysis, with the b- and y-ions that are generated in the collision cell shown in red and blue, respectively. As before, these ions were used for software based peptide sequencing and subsequent protein identification (3.3, 3.4, 3.5.2). Relative peptide and protein quantification could be carried out with the help of iTRAQ labels, with every reporter ion representing the relative abundance of the protein in either MAIT, NK or conventional CD8⁺ T (cCD8⁺) cells. The normalized intensity of these reporter ions was used to calculate three relative regulation factors, that display the relative abundance of

every protein in the different cell populations: MAIT:NK, MAIT:cCD8⁺ and NK:cCD8⁺. These three regulation factors (RF) can be calculated for every protein in every donor, resulting in 15 calculated RF for every protein. Again, these RF are displayed as log₂ values. An example of reporter ion intensities is also displayed in Figure 29. Here, the difference in abundance of the alpha chain of surface protein CD8 is shown. CD8 is a prototypic marker for cCD8⁺ T cells and a large subsets of MAIT cells. Accordingly, the highest abundance of this protein was detectable in cCD8⁺ T cells, and an almost equal amount could be identified in MAIT cells. NK cells only showed a low expression of CD8 (log₂ RF MAIT/NK: 1.13, MAIT/cCD8: -0.36, NK/cCD8: -1.48). As most of MAIT cells, and all cCD8⁺ T cells are positive for CD8, while NK cells show a variable expression,¹⁴⁴ these data is in accordance with expected values.

Analysis of the distribution of these regulation factors for every protein revealed a symmetrical distribution of the log₂ RF around the median, which is close to 0 in every case (Fig. 30). This distribution indicated that most identified proteins are not regulated in the different cell types. Importantly, it also becomes apparent that on, the level of the proteome, MAIT cells indeed are as different from cCD8⁺ T cells as cCD8⁺ cell from NK cells. Data also revealed that the distribution of the regulation factors is similar in every donor, with 50 % of all log₂ RF being distributed between roughly ± 0.2 , for MAIT:NK, MAIT:cCD8⁺ and NK:cCD8⁺, respectively. Only donor 2 showed donor variation and broader distribution of log₂ RF, with 50 % of all log₂ RF being distributed between ± 0.6 , ± 0.3 and ± 0.5 for MAIT:NK, MAIT:cCD8⁺ and NK:cCD8⁺, respectively.

Analysis of the donor specific patterns of the log₂ RF for every individual protein additionally revealed that all donors, except donor 2, depicted a highly similar regulation pattern, and displayed similar log₂ RF for the same proteins (Fig. 31). This again indicated high robustness of the acquired data. Donor 2 exhibited donor variation, with his proteins showing different log₂ RF values than the proteins of the other four donors.

Summarized, iTRAQ labels allowed relative quantification of protein abundance levels in MAIT, NK and cCD8⁺ T cells. This enabled the binary comparison of the pairs MAIT:NK, MAIT:cCD8⁺ and NK:cCD8⁺ and revealed consistent distribution of the calculated regulation factors, except for for some minor donor variations. Albeit these variations, no donor was excluded from the analysis as such donor variations have always to be considered when working with primary material. Most importantly, data also showed that MAIT cells are indeed a cell type as distinct from CD8⁺ T cells as from NK cells.

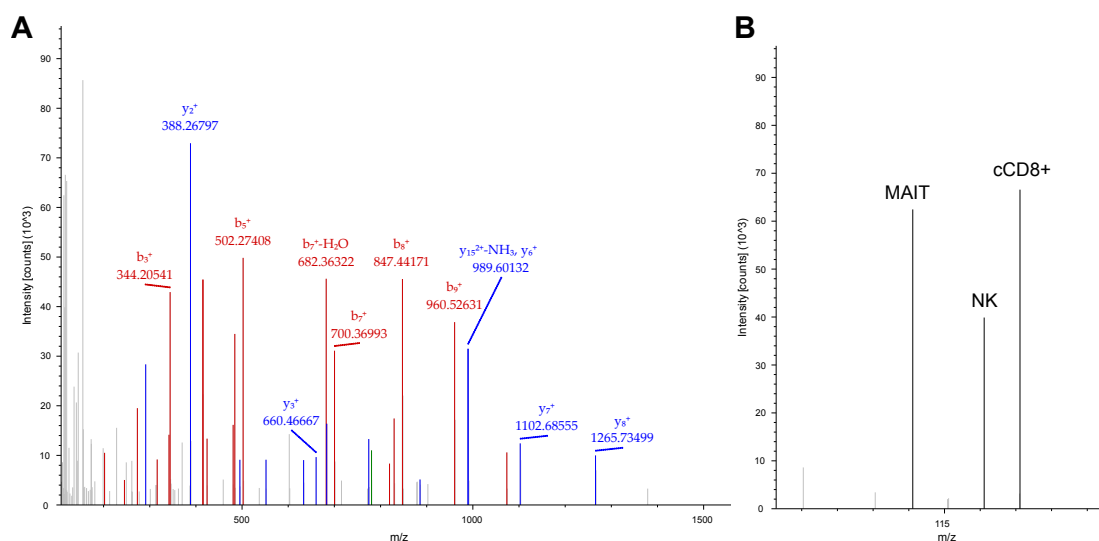


Figure 29 | MS/MS spectrum of an iTRAQ-labeled peptide of marker protein CD8, alpha chain. Proteins of MAIT, NK and cCD8⁺ T cells were digested with trypsin and labeled with different iTRAQ reagents. Labeled peptides were mixed and analyzed by mass spectrometry. In the mass spectrometer, peptides were fragmented and b- and y-ions generated (red and blue, respectively). Peptide sequence GAAASPTFLLYLSQNKPK could be derived from these ions through defined amino acid masses, and assigned to CD8 alpha chain. CD8 is a marker for CD8 T cells and expressed on large amounts of the MAIT cell population. Also smaller percentages of NK cells express CD8. Here, iTRAQ reporter ions with the masses 114 (MAIT), 116 (NK) and 117 (cCD8⁺), respectively, could be detected. The relative intensity of the reporter ions, as seen enlarged on the right side, can be used to comparatively quantify the amount of CD8 present in the different cell types. NK cells show the lowest abundance of this peptide and the respective protein, while MAIT and cCD8⁺ T cells contain roughly the same amount (\log_2 RF MAIT/NK: 1.13, MAIT/cCD8⁺: -0.36, NK/cCD8⁺: -1.48).

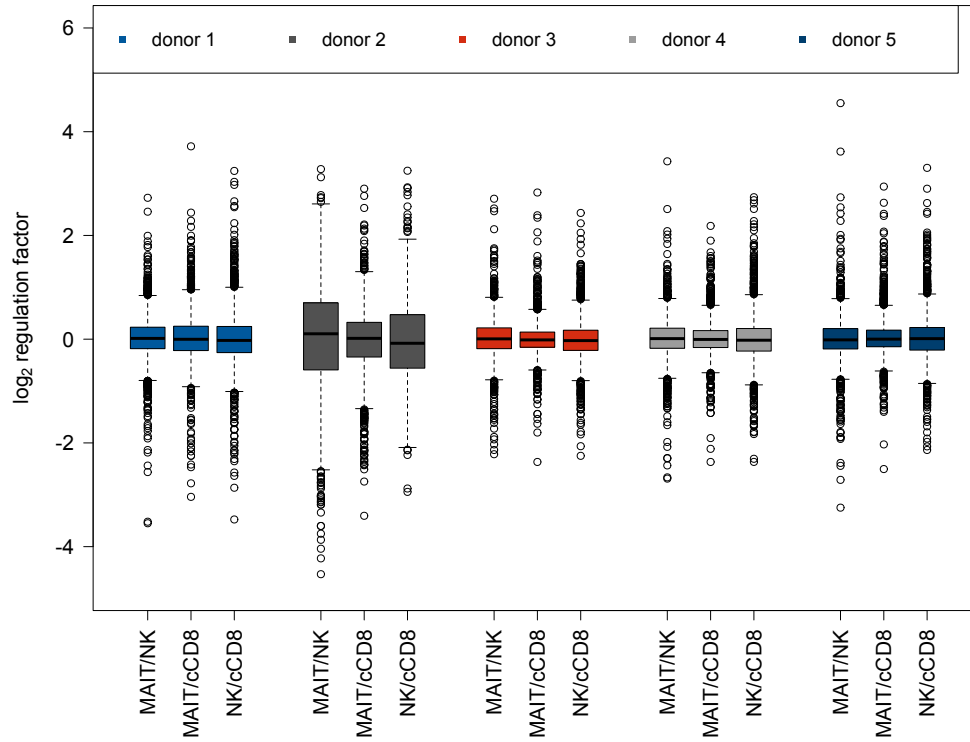


Figure 30 | Distribution of the regulation factors in five donors shows distinct differences between MAIT, NK and cCD8⁺ T cells. Human MAIT, NK and cCD8⁺ T cells were isolated from five different donors, and proteins were identified and quantified by mass spectrometry. The relative intensities are displayed as log₂ regulation factors. The thick line indicates the median and boxes the range that contains 50 % of the data, while the whiskers indicate the minimum and maximum of the data, as long these do not differ more than 1.5-fold as the interquartile distance from the median. Data points that lie outside this distance are considered as outliers and displayed as points. All donors show a symmetrical distribution of unregulated proteins around log₂ RF 0. The log₂ RF of donor 2, however, show a greater variation. In general, the log₂ RF already indicate that MAIT and cCD8⁺ T cells differ on the proteomic level, as well as MAIT and NK cells.

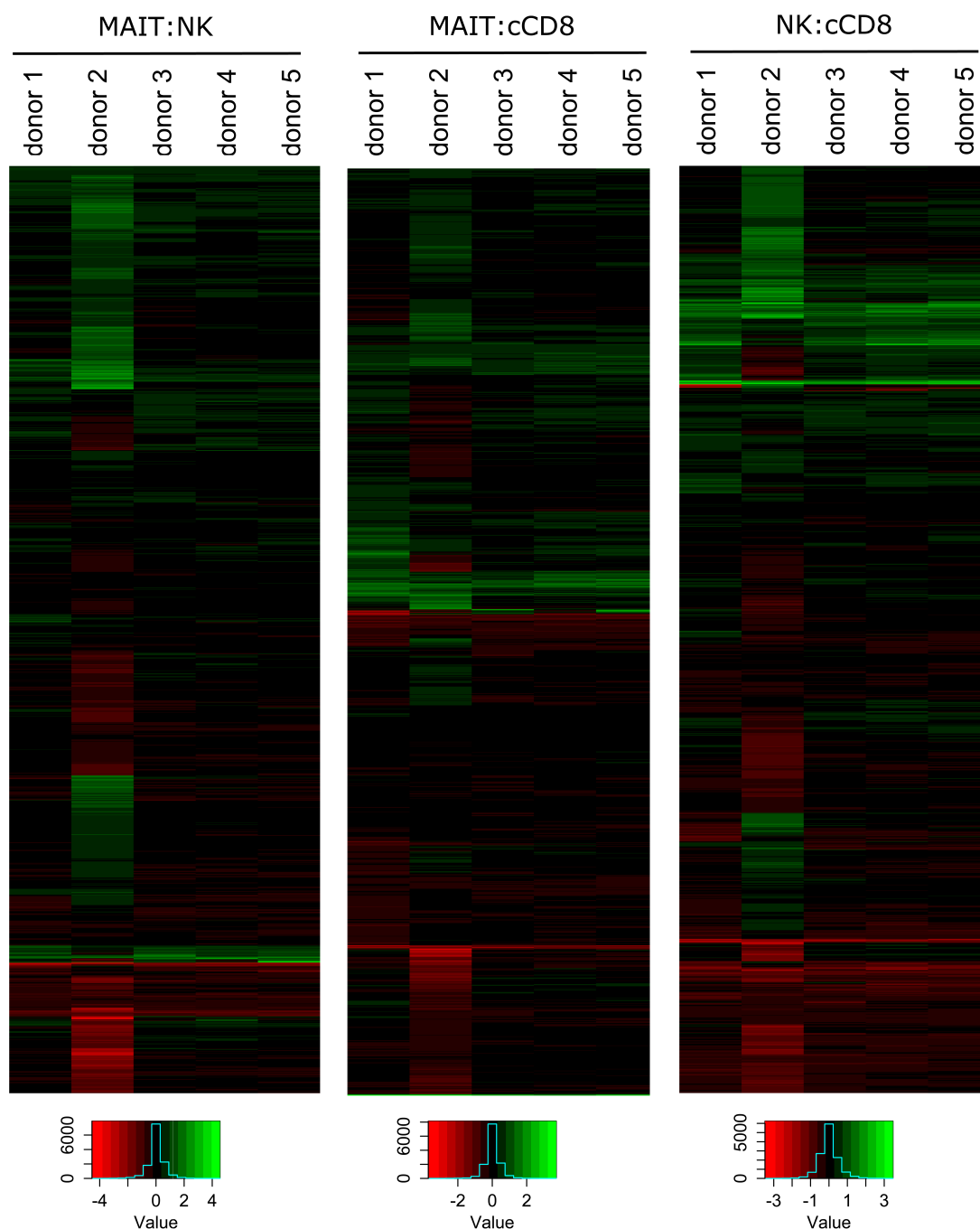


Figure 31 | Heat maps of log₂ regulation factors determined by iTRAQ-based LC-MS/MS from primary human MAIT, NK and cCD8⁺ T cells. 2619 proteins from primary human MAIT, NK and cCD8⁺ cells were identified and quantified by iTRAQ-based LC-MS/MS. Colored boxes in one row display the regulation of a single protein in five different human donors, and one column depicts protein regulations in one blood donor. The color code shows down-regulation as red, and up-regulation as green with the intensity of the color corresponding with the strength of the regulation. No regulation is depicted in black. Four donors show similar regulation patterns, while donor 2 shows distinct donor variation with substantial differences in regulation. Histograms below display the distribution of protein regulation factors and the corresponding color code.

3.5.3.2 Robust identification of regulated proteins in MAIT, NK and cCD8⁺ T cells indicates distinct proteomic profiles

Regulation factors (\log_2 RF) themselves already allowed estimations about the similarity and difference of the analyzed cell types. Robust identification of proteins with statistical differences in abundance between cell types, however, does not only help to refine the analysis of the relation of MAIT, NK and cCD8⁺ T cells. Also, it allows to check for individual marker proteins in every population, and to identify proteins that are vital for the MAIT cell phenotype and effector functions. Visible donor variations made a robust statistical method necessary, that allowed identification of significantly regulated proteins.

After calculation of the \log_2 RF for every protein in every donor, a statistical approach had to be used to determine the significantly regulated proteins between the cell types (2.8). In brief, it was assumed that the \log_2 regulation factors (RF) for each protein were following the normal distribution, with the same standard deviation for every protein. The Median Absolute Deviation from the median (MAD) of all detected proteins was then used to robustly estimate the standard deviation. This allowed the calculation of the probability if the \log_2 RF can be explained by the calculated standard deviation from the expected value. A protein was considered as significantly regulated if this probability was lower than 5 % in every donor. This means that when speaking of a regulated protein, usually a protein regulated in all five donors is meant, if not indicated otherwise.

With this method, 135 proteins were determined to be significantly regulated in all five donors when comparing MAIT and NK cells, 160 proteins for the MAIT:cCD8⁺ T cell comparison and 231 proteins were identified to be regulated between NK and cCD8⁺ T cells (Tab. 12). Between MAIT and NK cells, 77 proteins were significantly regulated up and 58 were regulated down, while in MAIT and cCD8⁺ T cells 110 were found to be upregulated and 50 downregulated. NK cells showed an upregulation of 113 proteins when compared with cCD8⁺ T cells, 118 proteins were downregulated. A summary of regulated proteins can be found in Table 13.

To check consistency and reliability of data, proof of concept proteins were checked for their regulation factors (Tab. 14), and if these \log_2 RF were in accordance with literature and expected data. Data in Table 14 show median \log_2 RF for several proteins. The number of experiments the protein was identified in is indicated by asterisk, while colored asterisks symbolize an experiment in which the protein was identified to be significantly regulated. Detected abundance of CD3 ϵ was in accordance with values expected after sorting, as cells were labeled for sorting with an antibody specific for CD3 ϵ . The differential expression of CD3 ϵ that cells were sorted on, with MAIT and cCD8⁺ T cells being positive and NK cells

Table 12 | Number of regulated proteins per compared cell types

identified regulated proteins			
	MAIT:NK	MAIT:cCD8 ⁺	NK:cCD8 ⁺
upregulated	77	110	113
downregulated	58	50	118
total	135	160	231

being negative for CD3 ϵ , could be detected in the mass spectrometer also. CD8 α chain was found to be higher expressed in MAIT and cCD8⁺ T cells as in NK cells, again proving that mass spectrometry is able to correctly detect differences of protein abundance that have been determined by cell sorting before. The same is valid for CD56, being highly expressed in NK cells. Large percentages of NK cells typically express high amounts of Fc receptor CD16 on the surface,¹⁷ also detectable in the present data set. CD26, a dipeptidyl peptidase, has recently been determined as a marker for MAIT cells,⁸² and its high, MAIT-specific expression also resulted in a substantial log₂ RF MAIT:cCD8⁺ of 2.39, and significant regulation. CD26 was also the protein with the highest median log₂RF between MAIT and cCD8⁺ T cells. Additionally, Dusseaux and colleagues already observed the high expression of multi-drug resistance transporter MDR1 in MAIT cells when compared with non-MAIT CD8⁺ T cells,⁸⁰ which could also be detected in this study with a log₂ RF MAIT:cCD8⁺ of 1.07. The same study reported that MAIT cells characteristically express low amounts of CD62L (L-selectin). Again, proteomic data showed the same result, with log₂ RF MAIT:cCD8⁺ of -2.43 and significant regulation in all donors the protein was identified in. The characteristically high abundance of intracellular perforin in NK cells¹⁴⁵ could also be detected with mass spectrometry. Summed up, semiquantitative mass spectrometry is a reliable tool for detecting differences in abundance of proteins, and used statistical methods are suitable to identify significantly regulated proteins in MAIT, NK and cCD8⁺ T cells. Generated data is in accordance with expected values, like CD3 ϵ or CD8 α , and data from literature, like CD26 or MDR1.

A recent study by Fergusson and colleagues has generated transcriptomic data, comparatively analyzing the difference between CD8⁺CD161⁻ T cells and CD8⁺CD161⁺⁺ T cells.¹⁴⁶ Almost all CD8⁺CD161⁺⁺ T cells are MAIT cells, and as the majority of MAIT cells analyzed in the proteomic study of this thesis (CD3⁺V α 7.2⁺CD161⁺⁺) are also CD8-positive, this transcriptomic comparison roughly matches the proteomic comparison between MAIT cells and cCD8⁺ T cells. To further verify the generated proteomic data, results of both studies were compared. In the transcriptomic study, 544 genes were found to be differentially regulated between MAIT

Table 13 | List of proteins regulated in all five donors

regulated proteins (UniProt ID)			
	MAIT:NK	MAIT:cCD8 ⁺ NK:cCD8 ⁺	
upregulated	DPP4, LAT1, ANXA5, OXLA, GRAK, GALK, LEG3, CASP1, CAH2, DREB, 4F2, EMAL4, THMS1, SCRN1, PDCD4, AMPD3, PRDX2, RASF2, SPEE, IPYR, STA5B, VIME, ENOG, GIMA4, ANM5, ARL3, GNAS2, SYK, CD48, CD59, ANXA2, PAIB3, RAB18, GBP2, HXK1, KS6A3, RL15, DDX47, RNT2, MMSA, PROF2, TBA4A, VWA8, NMT2, LR16C, PLEC, RL18, ALBU, ANXA1, PDK3, NOP58, NDRG1, GDIA, SND1, NEK7, LDHB, RL7, RLAO, ODO1, KPVM, RS3A, NOP56, DHPR, PUR9, RL10A, RL4, RL1D1, FBRL, DDX21, REEP5, RL7A, AB11, LPPRC, RL14, RL3, M4K1, LONM, TRAP1	DPP4, LAT1, OXLA, GRAK, GRAA, LEG3, S10A4, MYO1F, CYTF, ANXA2, S10AA, ANXA1, 4F2, CAH2, G1YG, SCRN1, CASP1, GRIN3, ACTN4, AT2B4, SYTL2, ERMPI1, GRAM, GALK, CATW, SC61B, ANXA5, GNS, UGDH, ANXA4, THIM, HEXB, CD47, MLEC, CD48, PDIA6, REEP5, S10AB, GBP5, RAB9A, PPG8, APMAP, TNAP3, HYOU1, DHRS7, STAT4, ADA10, RRAS2, ERG1, IFIX, ARL3, CATZ, JUND, EMAL4, BGAL, GNAS2, EFHD2, TBK1, ARP5L, AREG3, GDIA, CD44, GFRP, CAN2, RAB18, PBIP1, TMEDA, IGHG1, PTN4, PDIA1, SYNE2, STOM, EHD1, RAB7L, PP2BA, PDK3, GAPRI, GMPPB, NEK7, MYO5A, SC24C, GBB2, KCC2D, RAB6A, PI42A, MATK, SFXN3, CD59, UBAP1, OST48, PPIPI1, VINC, ENPL, COPG1, MKO1, KS6A3, SRPR, DDAH2, GMPPA, TRPV2, SH2D3, ALR, CIL42, 1A33, SYTL1, ABI3, CN159, VIGLN, DPP2	PERF, FCERG, GELS, CLIC3, DNS2A, CYTF, GRAB, IGHG1, ITAM, GRAH, EFHD2, CATW, CATC, PTN4, ITB2, AK1C3, ARP5L, DOK2, APOBR, GNS, ABC3G, SNX18, GAPRI, STX7, MYO1F, H15, TBX21, H31, RGS3, SH22A, NPC2, STOM, PCP, ANXA4, CYTSB, REL, RMD3, PTN12, IGKC, ICAM1, LAC2, DDAH2, PAXI, ASFG, A1AT, MPRI, LASP1, SH2D3, SIGIR, DGKQ, LIMD1, CD3Z, IFIX, TPM4, PDL1, NHRF1, CD97, ICAM3, OSTF1, MOES, NFAC2, VINC, CATZ, RRBPI1, SHIP1, SYTL2, ADA10, BAP18, ABI3, LPP IDUA, FHL3, PPR18, CASP3, DJB11, STK10, SNP29, AT2B4, PTPRJ, THTM, CC88B, PKHO2, UBP28, ARFP1, VP37B, GBP5, IFTT3, LAMP1, NUCB1, COR1C, MB12A, GPR56, SETD3, QKI, SNX3, TOR1B, BIN2, PICAL, LITAF, AREG3, LYAG, PRDX5, EPI5R, VASR, CALX, RUNX3, WIPF1, WASP, CATS, TRPV2, NEB2, PKHA2, SLK
downregulated	RAIX, LTOR5, COF1, SNX3, RABE2, MVP, MOES, EPI5R, CAPG, UBP28, VASP, DUS23, NHRF1, ARP5L, PAXI, APOBR, HBB, NFAC2, CASP3, NLTP, HN1, HBD, LIMD1, GAPRI, COR1C, HDDC2, REL, RGS3, DGKQ, LAC2, GPR56, DOK2, IKZF3, BAP18, LASP1, STMN1, IGKC, STX7, ABC3G, ITB2, PTN12, LEG1, EFHD2, TBX21, CATC, PDL1, H15, DNS2A, SNX18, AK1C3, CLIC3, GELS, ITAM, GRAB, FCERG, H31, PERF, GRAH	ECI2, PPT1, DDX24, AL9A1, XRCC5, CYTIP, XRCC6, SPB1, RL13A, RL28, RL7A, PUR8, RS7, EBP2, RL12, RL7, FLNB, RS11, ETFA, RL1D1, RS13, ARHGI, RL11, ANXA7, RL4, ABCE1, PDCD4, RS3, RL6, RL5, GRAP2, DDX18, IPYR, GNL3, NEPI, DKC1, DDX27, SRP14, PRKRA, HXK1, RS2, NOP56, RL34, RL10A, CH60, RL18, RS3A, RS16, RLAO, IPYR2, SPTN1, RS5, SYFB, FKBP5, DDX21, MDHC, TR112, PUR9, FBRL, AMPD3, KPVM, NOP58, DNPEP, RL15, TRAP1, M4K2, BRX1, RRP5, ESTD, ARH, MTAP, GIMA4, ISCA2, DHPR, BCI1B, PGK1, ADK, RPIA, APT, SPTB2, PLEC, GBPI, ANM5, SYFA, SAHH, SSDH, NPIL4, APEX1, 5NTD, VIME, THYN1, LHPF, ENOG, TALDO, ANXA5, SFXN1, PAIB3, PRDX1, KCC4, CD6, TBA4A, DDX47, SKAP1, KPCA, S100B, PROF2, CD5, PRDX2, DGKA, ACTN1, HYES, THMS1, SERA, RGS10, LDHB, COTL1, H10, CBR3	

Table 14 | Significantly regulated proof of concept-proteins in MAIT, NK and cCD8⁺ T cells

Protein name	log ₂ regulation factor median		
	MAIT:NK	MAIT:cCD8 ⁺	NK:cCD8 ⁺
CD3 epsilon chain ¹⁴⁴	1.70 ****	-0.07 ****	-1.76 ****
CD8 alpha chain ¹⁴⁴	1.28 ****	-0.24 ****	-1.59 ****
CD16a ¹⁴⁴	-2.88 ***	-0.05 ***	2.82 ***
CD26 ⁸²	2.61 *****	2.39 *****	-0.25 *****
CD56 ¹⁴⁴	-0.51 ***	0.44 ***	1.51 ***
CD62L ⁸⁰	-1,43 ***	-2,34 ***	-0,77 ***
MDR1 ⁸⁰	0,55 ****	1,07 ****	0,42 ****
Perforin ¹¹⁷	-2.30 *****	0.26 *****	2.74 *****

Asterisks indicate the number of experiments the protein was identified in. Asterisks in red and green indicate significant down- or upregulation.

cells and classic CD8⁺ T cells, identifying 195 upregulated genes and 349 as downregulated. For 160 of these genes the corresponding proteins were identified in the proteomic study of this thesis. The overlap of actually regulated proteins was 19. Accordingly, 141 proteins that were identified in both the transcriptomic and proteomic dataset, and assigned as regulated with transcriptomics were not identified as regulated in the proteomic study. Furthermore, none of the other proteins that were identified to be regulated in the proteomics study were found to be regulated on the transcriptomic level. Of the 19 genes and proteins that were found to be consistently regulated in both transcriptomic and proteomic analysis, data was in full accordance with all regulation factors showing the same tendency regarding up- and downregulation. Respective proteins are indicated with italics in Tab. 13. Taken together, the transcriptional data identify a different set of genes to be regulated between MAIT cells and cCD8⁺ T cells than the proteomics study. However, no contradictory data could be located in the proteins or corresponding genes that were found to be regulated in both studies.

In summary, the determination of the numbers regulated proteins yielded further information about the similarity and differences in human MAIT, NK and cCD8⁺ T cells, and indicated specific proteomic profiles for each of the subsets. Data was also in accordance with transcriptomic studies, and also the abundance of proof of concept and marker proteins was as expected.

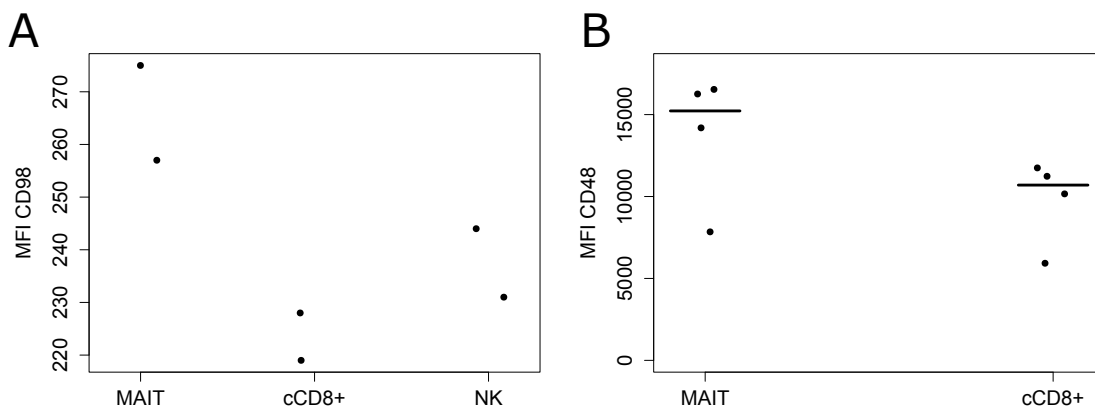


Figure 32 | Expression of CD48 and CD98 on MAIT, NK and cCD8⁺ T cells PBMCs were isolated from human donor blood, and expression of CD98 and CD48 were analyzed by flow cytometry (A and B, respectively). (A) Expression of CD98 is highest in MAIT cells, and lowest in cCD8⁺ T cells. (B) MAIT cells express more CD48 on their surface than cCD8⁺ T cells. Every dot represents one human donor, lines indicate the median.

3.5.3.3 Proteomic data is validated by flow cytometry

After checking if data was in accordance with expected values and recent literature (see 3.5.3.2), proteomic data was also to be complemented by flow cytometry. PBMCs were isolated from human donor blood (see 2.6.2), stained with antibodies and analyzed by flow cytometry. Abundance of the analyzed proteins was assessed by median fluorescence intensity (MFI) in the specific cell types. Cell types were gated as described before (see 3.5.1, Figure 25), proteins checked for surface and internal expression were CD48 and CD98. In the proteomic data set, CD98 was significantly regulated in all five donors between MAIT and NK cells, and MAIT and cCD8⁺ T cells with median log₂ RFs of 2.01 and 2.38, respectively, indicating a high abundance in MAIT cells. The log₂ RF NK:cCD8⁺ was determined to be 0.34. Flow cytometric data showed the same regulation (Fig. 32A), with the highest abundance detected in MAIT cells and the lowest in cCD8⁺ cells. The expression in NK cells is not significantly higher as in cCD8⁺ cells. CD48 showed a significant difference of protein abundance between MAIT and cCD8⁺ T cells, with a log₂ RF of 0.78. This increased amount of CD48 could also be detected in the flow cytometric analysis (Fig. 32B). Taken together, FACS analysis confirmed the difference of protein abundance that was determined by mass spectrometry before and further underlines reliability of the generated data.

3.5.4 Immunological effector proteins show distinct abundance in MAIT cells

3.5.4.1 MAIT cells possess a unique set set of effector molecules

After isolation of the cells from human donor blood, 2600 proteins were identified from human MAIT, NK and non-MAIT CD8⁺ T cells (cCD8⁺ cells), and several hundred were identified to be regulated when comparing the abundance in the different cell types with iTRAQ-based relative quantification (3.5.2, 3.5.3.1, 3.5.3.2). Several specific markers could be identified, but the abundance of effector molecules which MAIT cells realize their unique functions has not been assessed proteomically.

Interestingly, several important immunological effector molecules were among those regulated proteins, and all five human granzymes (A, B, H, K, M, see Tab. 15). Granzyme A was upregulated in MAIT and NK cells, when compared with cCD8⁺ cells, while Granzyme B showed the highest abundance in NK cells and was equally abundant in MAIT and cCD8⁺ T cells. Granzyme H was also highest expressed in NK cells, but showed significant regulation between MAIT and cCD8⁺ T cells also, being downregulated in MAIT cells. Granzyme K was highly abundant in MAIT cells, and identically expressed in NK and cCD8⁺ T cells. Also the abundance of cytolytic protein granulysin, that had been shown to be expressed in MAIT cells before could be detected. Granulysin abundance, however, was lower than in NK cells, and similar to cCD8⁺ T cells, like the other major cytolytic protein perforin (3.5.3.2, Tab. 14). The expression and secretion of granzymes A, B and K in MAIT cells has recently been analyzed by flow cytometry.^{80,117} FACS data also showed an increased expression of closely related granzymes A and K in MAIT cells when compared with cCD8⁺ T cells, but also indicated a small population expressing granzyme B in cCD8⁺ T cells.¹¹⁷ This difference was not detected in the proteomic dataset.

These data indicate a specific immunological phenotype for MAIT cells that is realized through differential expression of immunological active proteins. MAIT cells possess a different arsenal of effector molecules, enabling them to execute functions that vary from innate NK cells but also closely related conventional, non-MAIT CD8⁺ T cells. This phenotype is most likely heavily dependent on closely related granzymes A and K, that are both serine proteases. Interestingly, MAIT cells also express granzyme M in larger amounts than cCD8⁺ T cells, but still lower amounts than the innate NK cells.

Table 15 | Regulation of effector molecules in MAIT, NK and cCD8⁺ T cells

Protein name	log ₂ regulation factor median		
	MAIT:NK	MAIT:cCD8 ⁺	NK:cCD8 ⁺
Granzyme A	-0.08 *****	1.60 *****	1.78 ***** *
Granzyme B	-2.08 *****	0.05 *****	1.82 *****
Granzyme H	-2.44 *****	-0.71 *****	1.64 *****
Granzyme K	1.66 *****	1.91 *****	0.29 *****
Granzyme M	-0.84 ***** *	0.92 *****	1.90 ***** *
Granulysin	-1.82 *****	0.28 *****	2.13 *****

Asterisks indicate the number of experiments the protein was identified in. Asterisks in red and green indicate significant down- or upregulation.

3.5.4.2 Proteins regulating exocytosis and proliferation are upregulated in MAIT cells

Distinct proteomic profiles, especially of immunologically active effector molecules in MAIT, NK and conventional CD8⁺ T cells (cCD8⁺ T cells, 3.5.4.1) already indicated a MAIT specific phenotype. One of the most important questions, however, still remains: what determines the distinct phenotype of MAIT cells, when compared with cCD8⁺ T cells? Do they exert different functionality, that has not been discovered yet? To be able to answer these questions, it is necessary to not exclusively look for effector proteins that are already known to be important. Rather, systematic analyses have to be executed, allowing to determine whole processes that show different abundances in MAIT cells than in cCD8⁺ T cells.

Bioinformatical tools like Pathway Studio or Gene Go make it possible to analyze the enrichment of proteins that are associated with specific pathways or cellular functions. To further investigate the innate-like phenotype of MAIT cells, and analyze the consequences of protein regulation, the list of proteins that were found to be upregulated in all five donors were loaded into GeneGo analysis tool (Thomson Reuters). To gain knowledge about processes that are typical for MAIT cells, and additionally distinguish them from cCD8⁺ T cells the analysis was focused on the proteins that were highly upregulated in MAITs when compared to cCD8⁺ T cells, meaning regulated with a median log₂ RF of 0.8 or higher (Fig. 33). These proteins were annotated to GeneGo molecular processes. Interestingly, all except one of the top ten pathways that were found to be upregulated and therefore

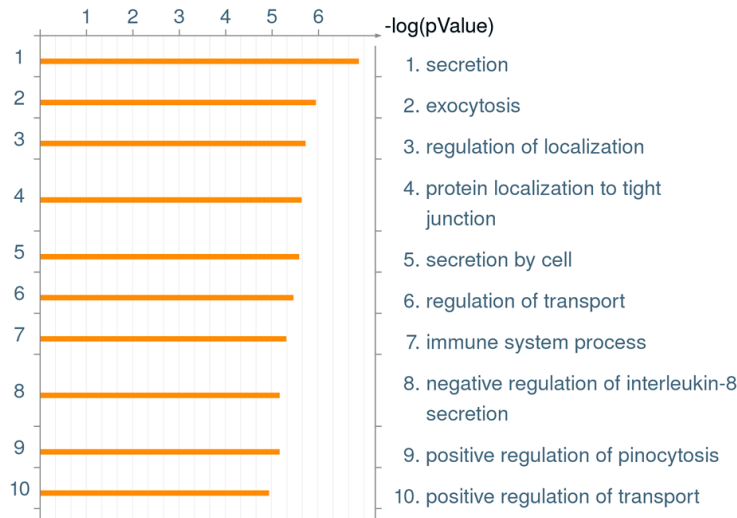


Figure 33 | GeneGo enrichment analysis of MAIT proteins, compared to cCD8⁺ T cells. Proteins being upregulated between MAIT and cCD8⁺ T cells in all five donors, with a minimum median log₂ RF of 0.8 were checked for pathway enrichment in GeneGo analytical software. Coverage of the pathways is calculated as *p*-value, here shown as negative logarithm. Analysis shows enrichment of pathways connected to transport, secretion and exocytosis.

enriched in MAIT cells were associated with secretion, transport and exocytosis. The strong upregulation of proteins annotated to these processes indicates that the transport and secretion system of MAIT cells might play a pivotal role in these cells. Proteins associated with the GO pathway exocytosis are shown in Table 16, all of them have been shown to promote exocytosis. For example, secernin-1 (median log₂ RF MAIT:cCD8⁺ 1.07, MAIT:NK 0.94) has been shown to increase both the extent of secretion in mast cells, and the sensitivity of mast cells to stimulation with calcium.¹⁴⁷ Its pronounced abundance in MAIT cells might be an indicator for a crucial role of this protein in the MAIT cell phenotype, and might result in MAIT cells being not only very sensitive for stimulation but secernin-1 might also boost the secretion of this innate-like T cell subtype. Alpha-actinin 4 (median log₂ RF MAIT:cCD8⁺ 1.07) is an calcium-dependent actin-binding protein mediating interactions between the membrane and actin filaments.¹⁴⁸ Annexin IV (median log₂ RF MAIT:cCD8⁺ 0.81) has also been shown to play a role in exocytotic processes, involving neuronal synapses where it associates with synaptotagmin.,¹⁴⁹ while unconventional myosins like myosin-If (median log₂ RF MAIT:cCD8⁺ 1.39) are suspected to share similar properties to myosin, which is an actin-dependent motor protein.¹⁵⁰ Synaptotagmin-like protein 2 (Slp2, median log₂ RF MAIT:cCD8⁺ 0.96) contributes to secretory lysosome exocytosis from cytotoxic lymphocytes and has been shown to be associated with the immunological synapse.¹⁵¹

Strikingly, calcium-binding protein S100A4 was also identified to be highly abundant in MAIT cells, when being compared with both cCD8⁺ T cells and NK cells (median log₂ RF MAIT:NK 1.06, MAIT:cCD8⁺ 1.43). In a previous study it could be shown that S100A4 is highly expressed in a cytotoxic NK cells subset,¹⁹ and has been discussed as being pivotal for NK cell cytotoxicity and directed granule exocytosis (M. Heyner, unpublished data).

Table 16 | Proteins strongly upregulated in MAIT:cCD8⁺ and associated with GeneGo molecular process “exocytosis”

Protein name	log ₂ RF median		
	MAIT:NK	MAIT:cCD8	NK:cCD8
Alpha-actinin 4	-0.27	1.03 *****	1.29 *****
Annexin IV	-0.31	0.81 *****	1.25 *****
Unconventional myosin-If	-0.13	1.39 *****	1.32 *****
Secernin-1	0.94 *****	1.07 *****	0.10
Synaptotagmin-like protein 2	0.07	0.96 *****	0.82 *****

All proteins were identified in all five donors. Asterisks indicate the number of donors the proteins was identified as regulated in.

When having a look at the twenty strongest regulated proteins between MAIT and cCD8⁺ T cells, more proteins associated with exocytosis appear, like annexin 2 or cystatin-F (Tab. 17). Also, effector proteins like granzyme A and K are among the proteins with the highest difference in abundance. Interestingly, also proteins that are annotated with regulation of proliferation like CD98, L-amino-acid oxidase and galectin-1 are expressed in much higher amounts in MAIT cells than in cCD8⁺ T cells. High abundance of these proteins indicates distinct regulation of proliferation in MAIT cells. The protein identified with the highest difference in abundance is CD26, a MAIT cell marker.⁸²

More evidence for a pivotal role of proteins like CD98, L-amino-acid oxidase, secernin-1, and annexins in the definition of MAIT cells phenotype becomes apparent when investigating the proteins that are exclusively upregulated in MAIT cells (Tab. 18). The first eleven proteins on this list overlap with Table 17, this prominent abundance in MAIT cells when compared with the other analyzed cells underlining their potential importance for the innate-like MAIT cell phenotype. Functional annotation of the proteins that had not been covered in Table 17 revealed association with various different functions, like Ras/Rab-signaling (UniProt accessions P63092, P31150, Q9NP72), metabolic processes (Q96C23, Q15120) or T cell activation (P09326/CD48). Additionally, proteins linked to reorganization of microtubules (Q9HC35, Q8TDX7) and proliferation (P51812) could be identified, as well as anti-coagulant annexin V and the inhibitor of the complement system CD59. Importantly, all these proteins can potentially serve as markers to discriminate MAIT cells from conventional CD8 T cells, due to their increased abundance in the former.

Table 17 | Top twenty regulated proteins between MAIT cells and cCD8⁺ T cells

Protein name	log2 RF median		
	MAIT:NK	MAIT:cCD8	NK:cCD8
Dipeptidyl peptidase 4 (CD26)	2.61	2.39	-0.25
Large neutral amino acids transporter subunit 1 (CD98)	2.01	2.38	0.37
L-amino-acid oxidase	1.82	2.00	0.02
Granzyme K	1.66	1.91	0.29
Granzyme A	-0.08	1.60	1.78
Galectin-3	1.19	1.49	0.05
<i>Protein S100-A4</i>	<i>1.06</i>	<i>1.43</i>	<i>0.42</i>
<i>Unconventional myosin-If</i>	<i>-0.13</i>	<i>1.39</i>	<i>1.32</i>
<i>Cystatin-F</i>	<i>-0.63</i>	<i>1.33</i>	<i>1.93</i>
Annexin A2	0.75	1.32	0.59
Protein S100-A10	0.92	1.30	0.25
<i>Annexin A1</i>	<i>0.63</i>	<i>1.22</i>	<i>0.61</i>
4F2 cell-surface antigen heavy chain (CD98)	1.06	1.14	-0.03
Carbonic anhydrase 2	1.16	1.08	-0.19
Glycogenin-1	0.76	1.07	0.42
<i>Secernin-1</i>	<i>0.94</i>	<i>1.07</i>	<i>0.10</i>
Caspase-1	1.17	1.04	0.15
G protein-regulated inducer of neurite outgrowth 3	0.45	1.03	0.39
<i>Alpha-actinin-4</i>	<i>-0.27</i>	<i>1.03</i>	<i>1.29</i>
Plasma membrane calcium-transporting ATPase 4	0.38	0.98	0.72

Italic font indicates association with exocytotic processes.

In summary, highly upregulated proteins between MAIT and cCD8⁺ T cells show strong association to exocytosis and secretion. Interestingly, these are mostly proteins like secernin-1 that actively promote secretion, or proteins that can directly be associated with the formation of synapses. Additionally, the activity of all the proteins is influenced by calcium, a vital messenger during T cell activation. Furthermore, a set of proteins with pronounced abundance in MAIT cells was identified, that partly overlaps with the aforementioned proteins highly upregulated between MAIT and cCD8⁺ T cells. This list additionally includes proteins with a variety of different functions, like coordinating Ras/Rab-signaling, metabolic processes or microtubule reorganization.

3.6 First-time characterization of the MAIT cell immunological synapse

3.6.1 Formation of the MAIT immunological synapses

Although the cellular functions of MAIT cells have been investigated quite thoroughly, the molecular mechanisms coordinating their effector functions still need to be elucidated. MAIT cells are T cells after all, so the signaling pathways that result in activation might be very much the same as in conventional T cells. MAIT cells however, have a innate-like immunological function that is different from conventional cytotoxic T cells and has a far broader spectrum of possible targets. Also, MAIT cells showed increased abundance of proteins regulating exocytosis, like secernin-1 or S100A4. This indicates that their effector functions can be coordinated differently. How MAIT cells form the interface with the target cells, the so-called immunological synapse (IS), a contact that subsequently results in the death of the target cell, has not been investigated at all.

MAIT cells can be activated with antigen-presenting cells. Here, PBMCs were isolated from the blood of healthy human donors (2.6.2), and cells were stained with antibodies against CD161 and V α 7.2. CD3 was not stained to prevent overloading the cells with antibodies and effectively blocking fluorescence channels at the microscope with antibodies that were used for sorting and are still fluorescent and attached to the cells. Additionally, 95 % of V α 7.2⁺CD161⁺⁺ cells are also positive for CD3. For this experiment, MAITs were therefore defined as V α 7.2⁺CD161⁺⁺ cells and sorted by flow cytometry (2.6.3). Sorted MAIT cells were co-incubated with monocytic THP-1 cells that had been fed with fixed *E. coli* over night before for different time periods on cover slips. Cells were then fixed, permeabilized and stained with DAPI (4',6-diamidino-2-phenylindole) and various antibodies. Slides were analyzed on a Nikon inverted fluorescence microscope (2.6.4).

Table 18 | Proteins exclusively upregulated in MAIT cells

Protein name	log ₂ RF		
	MAIT:NK	MAIT:cCD8 ⁺	NK:cCD8 ⁺
Dipeptidyl peptidase 4 (CD26)	2.61	2.39	-0.25
Large neutral amino acids transporter small subunit 1 (CD98)	2.01	2.38	0.37
L-amino-acid oxidase	1.82	2.00	0.02
Granzyme K	1.66	1.91	0.29
Galectin-3	1.19	1.49	0.05
Annexin A2	0.75	1.32	0.59
Annexin A1	0.63	1.22	0.61
4F2 cell-surface antigen heavy chain (CD98)	1.06	1.14	-0.03
Carbonic anhydrase 2	1.16	1.08	-0.19
Secernin-1	0.94	1.07	0.10
Caspase-1	1.17	1.04	0.15
Aldose 1-epimerase	1.40	0.90	-0.40
Annexin A5	1.92	0.85	-0.93
CD48 antigen	0.76	0.78	0.06
Receptor expression-enhancing protein 5	0.48	0.78	0.13
ADP-ribosylation factor-like protein 3	0.77	0.70	-0.30
Echinoderm microtubule-associated protein-like 4	0.97	0.68	-0.43
Guanine nucleotide-binding protein G(s) subunit alpha isoforms short	0.76	0.67	-0.09
Rab GDP dissociation inhibitor alpha	0.60	0.65	-0.22
Ras-related protein Rab-18	0.73	0.63	0.17
[Pyruvate dehydrogenase (acetyl-transferring)] kinase isozyme 3	0.63	0.56	-0.33
Serine/threonine-protein kinase Nek7	0.59	0.54	-0.15
CD59 glycoprotein	0.75	0.50	-0.23
Ribosomal protein S6 kinase alpha-3	0.72	0.44	-0.19

All listed proteins are upregulated in MAIT cells, when compared with both NK and cCD8⁺ T cells.

To visualize the interface between MAIT cell and the target cell, samples were stained with DAPI and for perforin. DAPI is a fluorescent stain for DNA¹⁵² and perforin a lytic, pore-forming protein and key effector molecule for T-cell- and natural killer-cell-mediated cytotoxicity.¹⁵³ It is located in lytic granules, and can therefore serve as a marker. After establishing contact with THP-1 target cell, immunofluorescence microscopy shows MAIT cells to polarize (Fig. 34). While unstimulated MAIT cells show an equal spreading of lytic, perforin-containing granules (Fig. 34A), MAIT cells in contact with a THP-1 target cell quickly establish a polarization and the lytic granules are located at the IS (Fig. 34B).

To summarize, MAIT IS formation and degranulation could be documented for the first time. Translocation of perforin-containing granules toward the interface between MAIT cell and target cell is in perfect accordance with the cellular cytotoxicity that MAITs exert against their target cells.⁹⁴

3.6.2 S100A4 is associated with microtubules in MAIT cells

Calcium-binding protein S100A4 was found to be highly upregulated in MAIT cells when compared to conventional CD8⁺ T cells and even NK cells (15). S100A4 has also been shown to locate to the NK cell synapse after activation¹⁹ and might play a role in coordinating directed granule release in NK cells (M. Heyner, in preparation). Therefore, it was of interest to investigate if highly upregulated S100A4 also plays a role in MAIT cells. Furthermore, it has also been speculated that S100A4 can colocalize with microtubules in activated primary human T cells (N. Amsberg, personal communication). However, when analyzing MAIT cells regarding the subcellular localization of S100A4, it was not only of interest to investigate the association of S100A4 with the MAIT:target cell interface.

Microscopic imaging of localization of S100A4 in sorted MAIT cells (2.6.3, 2.6.4) also revealed a not strictly cytosolic distribution of the protein. S100A4 localization was instead rather focused on specific areas, and showed formation of defined structures (Fig. 35A). Analysis of microtubule formations in MAIT cells did not show colocalization of both proteins (Fig. 35B), but rather formation of common connected structures and a close association of both molecules (Fig. 35D).

To further investigate these structures, and their possible involvement in the formation of the MAIT IS, sorted MAIT cells were incubated with THP-1 cells that had been fed with *E. coli* before. Samples were then fixed, permeabilized, stained with DAPI and antibodies against α -tubulin and S100A4 and analyzed with a wide-field fluorescence microscope (Fig. 36). Interestingly, analysis of S100A4 localization in MAIT cells in contact with a target cell for fifteen minutes revealed not only high abundance of S100A4 in the MAIT cells, but also accumulation of S100A4 at the interface between MAIT cell and target cell (Fig. 36A). Staining

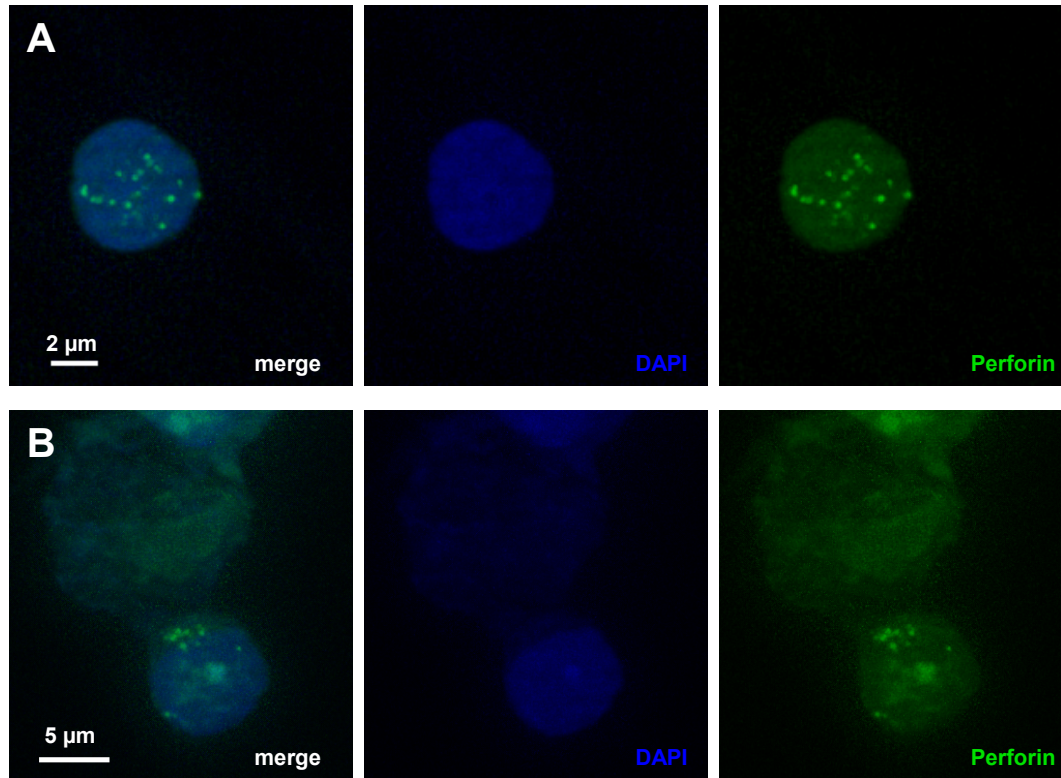


Figure 34 | Formation of the MAIT immunological synapse. Sorted MAIT cells were co-incubated with THP-1 cells that had been fed with fixed *E. coli* before. Cells were then fixed, permeabilized and stained with DAPI and monoclonal antibody against pore-forming protein perforin. Microscopical analysis was carried out on an inverted fluorescence microscope. Every image depicts the maximum intensity projection of a z-stack, displaying the maximum intensities of the layers of the whole z-stack as one 2D image. (A) shows a single non-polarized MAIT cell, with lytic granules containing perforin distributed equally in the cytoplasm. (B) displays an activated MAIT cell in contact with the THP-1 target cells, the lytic granules now polarized and localized at the immunological synapse.

of α -tubulin and microtubules showed that after fifteen minutes, the microtubule organizing center (MTOC) had relocated to the interface between MAIT cell and target cell (Fig. 36B). Noticeably it became visible that under these circumstances, S100A4 and microtubules show a partial colocalization (Fig. 35, arrows). S100A4 does not completely colocalize with α -tubulin and vice versa, but S100A4 is visibly partially located along microtubules.

In summary, partial colocalization of S100A4 and microtubules could be observed in activated MAIT cells. In MAIT cells without contact with a target cells, S100A4 is also located close to microtubules although no overlap or colocalization could be detected. Rather, a close association of both proteins could be observed. Hence, S100A4 localization is apparently coordinated by microtubules, and might even be recruited to the cytoskeleton upon activation. However, it became apparent that S100A4 might also indeed move to the interface between MAIT cell and target cell, when the MAIT cell is in an activated cell, and might therefor be a factor influencing formation of the MAIT IS.

3.6.3 S100A4 localizes at the MAIT IS in a time-dependent manner

MAIT cells form immunological synapses upon contact with target cells. S100A4 is a calcium-dependent protein, that has been shown to coordinate NK cell degranulation (M. Heyner, in preparation), and is highly upregulated in MAIT cells. Upon activation with a target cell, S100A4 can associate with microtubules and also localize to the interface of MAIT cell and target cell.

To further investigate a possible role of S100A4 in MAIT cell immunological synapse (IS) formation, sorted MAIT cells were incubated with *E. coli*-fed THP-1 cells, and settled on cover slips for different time periods. Samples were then fixed, permeabilized, stained with DAPI and antibodies against perforin and S100A4 and analyzed on a fluorescence microscope (2.6.3, 2.6.4).

Microscopic analysis revealed increased localization of S100A4 at the interface between MAIT cell and target cell. While non-activated MAIT cells show an equal distribution of S100A4 in the cell body (Fig. 37A), significantly higher abundance of S100A4 can be detected at the interface of MAIT cells and THP-1 target cell (Fig. 37B). This becomes even more apparent in plots that graphically display the intensity of fluorescence detected of the secondary antibody that is bound to S100A4 (Fig. 37C, D). The by far highest intensity is localized in the polarized cells at the immunological synapse. To verify these data, intensity in the respective channel of S100A4 was measured in several cells at different time points (Fig. 37E). Intensity was measured on a straight line, directed from the cell side not in contact with the target cells towards the IS (see schematic in Fig. 37E). Values are displayed as percent of intensity relative to the maximal intensity of all cells and time points were analyzed.

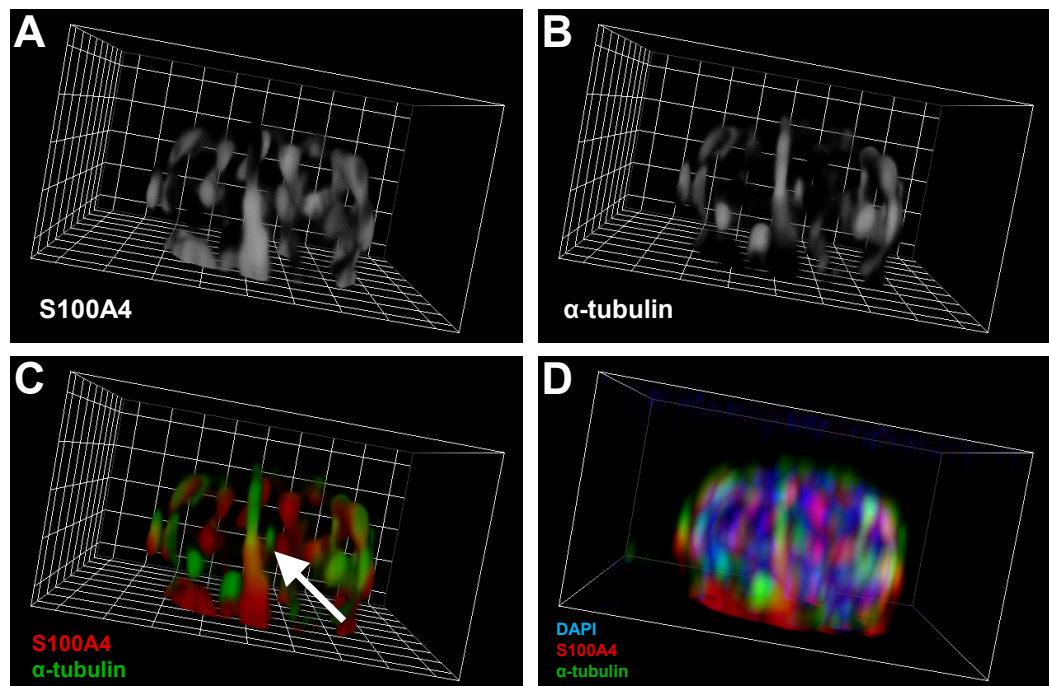


Figure 35 | S100A4 forms structures with microtubules in MAIT cells. Sorted MAIT cells were fixed, permeabilized, stained with DAPI and antibodies against α -tubulin and S100A4. Images were acquired by wide-field fluorescence microscopy, and deconvoluted afterwards with NIS-Elements software. Z-stacks were recorded and are displayed as a 3D model using perspective projection. Deconvoluted single channels images of S100A4 and α -tubulin (A, B) do not show colocalization of these proteins. Merged channels however reveal a formation of structures of S100A4 and microtubules, and close associations of these proteins (C, arrow). (D) shows a merged image of all channels. One graticule is 1 μ m. Different blending modes for creating the 3D image are used in A, B, C (alpha blending) and D (MaxIP). While alpha blending uses physical principles of light absorbing to accentuate object surfaces, MaxIP displays only pixels with the highest intensity values of the Z-sequence.

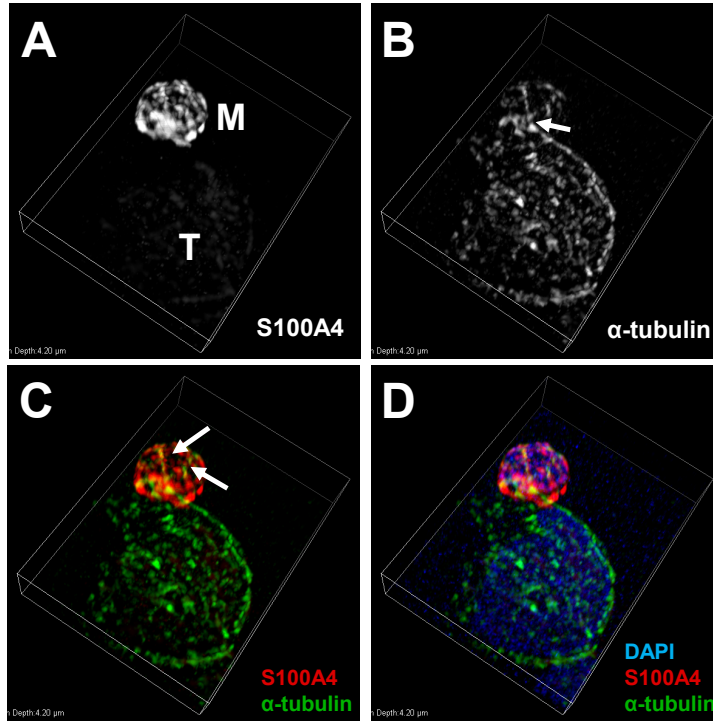


Figure 36 | S100A4 recruitment towards microtubules and the immunological synapse upon activation. Sorted MAIT cells were co-incubated with THP-1 cells that had been fed with fixed *E. coli* before. Cells were then fixed, permeabilized and stained with DAPI and monoclonal antibodies against α -tubulin and S100A4. Images were acquired by wide-field fluorescence microscopy, and deconvoluted afterwards with NIS-Elements software. Z-stacks were recorded and are displayed as a 3D model using perspective projection. Images display a MAIT cell (M) and associated target cell (T) after 15 minutes of co-incubation. (A) Single channel image of S100A4, showing accumulation of S100A4 at the interface between MAIT cell and target cell. (B) Single channel image of α -tubulin, showing the microtubule-organizing center (MTOC, arrow) located at the immunological synapse. (C) Merge of S100A4 (red) and α -tubulin (green). Note the overlap of both proteins on microtubules that originate at the MTOC (arrows). (D) Merge of DAPI (blue), S100A4 (red) and α -tubulin (green).

Interestingly, most unstimulated cells are also slightly polarized, displaying an unequal distribution of S100A4. When in contact with the target cell, however, this polarization increases drastically after 2 and 5 minutes, with large amounts of S100A4 relocating to the immunological synapse. This is accompanied by a loss of intensity of S100A4 signal at the side of the cell opposite from the IS. The intensity at the IS, at roughly 5 - 6 μm after start of measurement, does not only significantly increase, but also shows a broader distribution, indicating a larger area on which the present S100A4 is spread. After 10 and 30 minutes, intensity of S100A4 is distributed more equally again, indicating the dissolution of the immunological synapse. Interestingly, data also indicate an accumulation of target cell S100A4 on the target cell's side of the IS. This is displayed by the intensity peak that can be seen shortly behind the peak on the MAIT cell side.

In summary, microscopical analyses strengthen the evidence for a possible role of S100A4 in the MAIT phenotype. Proteomic data already showed a high upregulation of S100A4 in MAIT cells, implying an importance of this protein in the phenotype of MAIT cells. Now it could be shown that indeed S100A4 localizes at the immunological synapse of MAIT cells after activation with target cells, in time dependent manner.

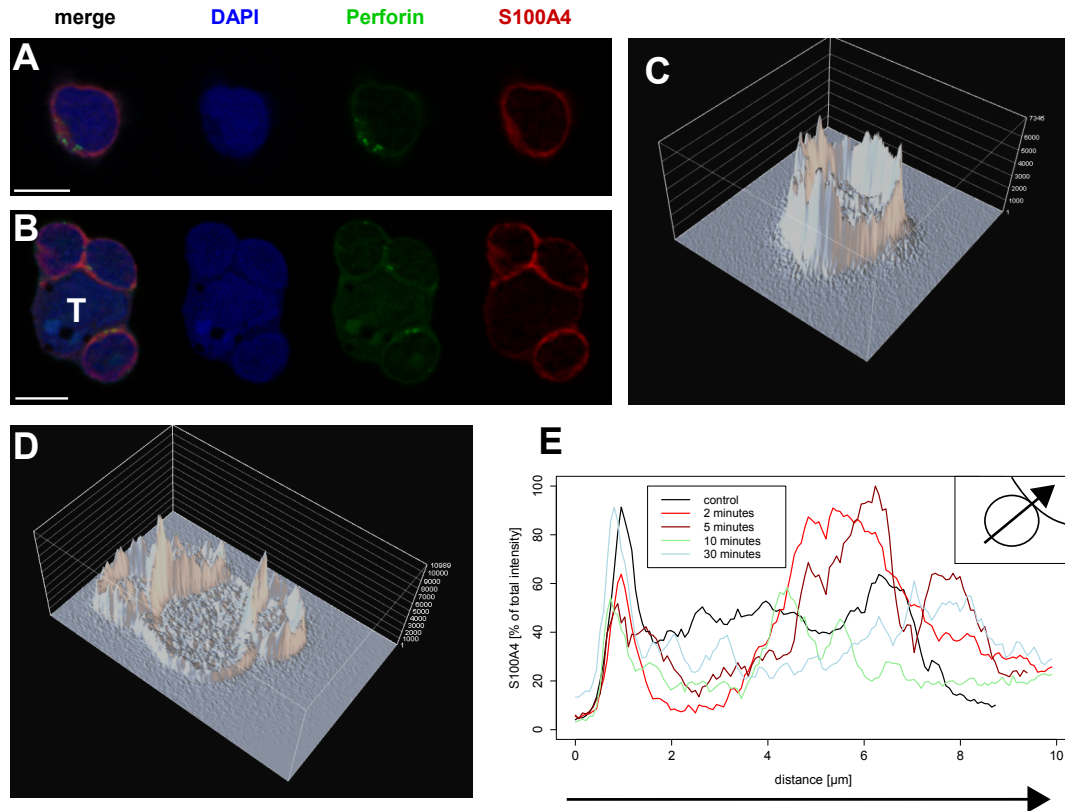


Figure 37 | S100A4 localizes at the MAIT immunological synapse. Sorted MAIT cells were co-incubated with THP-1 cells that had been fed with fixed *E. coli* before. Cells were then fixed, permeabilized and stained with DAPI and monoclonal antibodies against IS marker perforin and S100A4. Images were acquired by wide-field fluorescence microscopy. (A) A MAIT cell that is not in contact with a target cell. Although perforin appears to be localized in one spot, the distribution of S100A4 is spread through the whole cell. (B) MAIT cells in contact with a target cell (T) after five minutes of incubation. Lytic granules and high amounts of S100A are located at the interface between MAIT cell and target cell. (C & D) Intensity Surface Plot of the S100A4 channel (A) and (B), respectively. The higher the intensity of the detected S100A4, the higher elevation of the surface plot. Again, high abundance of S100A4 can be detected at the MAIT-target cell interface. (E) Development of S100A4 localization is displayed over the course of 30 minutes of IS formation. S100A4 intensity was measured on one line diametrical towards the immunological synapse, as displayed in the schematic. The intensity of S100A4 at the synapse at roughly 5-6 μm after the start of the measurement increases after IS formation, and peaks at 5 minutes. Afterwards, it decreases again. Scales in the microscopic images display 5 μm . Graph contains data from 33 cells and cell:cell conjugates.

4 Discussion

4.1 Chemical inhibition of NK cell effector functions

4.1.1 Specificity of used kinase inhibitors

The first part of this thesis showed the modulation of innate immune functions of NK cells with small chemicals (3.1.1, 3.1.2).¹³⁵ It could be shown that used inhibitors significantly reduced NK cell effector functions degranulation and cytokine release. However, although kinase inhibitors have been established as valid tools for enzyme inhibition in particular at the level of primary human immune cells,¹⁵⁴ their specificity, and thus their suitability to investigate the role of the target kinases has to be taken into account to interpret the results. Dasatinib inhibits not only the activity of Src-family kinases (SFKs) but also interferes with activity of kinases like BCR-ABL1, and is a valuable drug in leukemia therapy.¹⁵⁵ Dasatinib is indeed a proper tool for proof-of-concept experiments, as its targets, SFKs, are putative signaling components in NK cell activation.^{21,25} This could already been shown in previous studies, where application of Dasatinib diminished NK cell effector functions.^{156–158} The results generated in this thesis were not only in full accordance with the former studies, but also showed a strong impact of Dasatinib treatment on NK cells degranulation and TNF- α release in PBMC and pure NK cell cultures. A study by Hassold and colleagues, however, revealed that NK cells that were pretreated with Dasatinib for 24 hours showed increased effector functions.¹⁵⁹ This might be a mechanism of NK cells to adapt to Dasatinib exposure.

In contrast to Dasatinib, CK59, and CID755673 are considered as highly specific kinase inhibitors. CK59 has a structure analogue to kinase inhibitor olomoucine, which was demonstrated to specifically inhibit isoforms of CaMKII. Affinity studies revealed isoforms CaMKII- γ and CaMKII- δ to bind to CK59 with the highest affinity.¹⁶⁰ The same study also showed that 10 μ M CK59 already diminish activity of CaMKII to 45 %. Additionally, Poggi and colleagues demonstrated that inhibiting CaMKII activity reduces NK-cell killing of dendritic cells (DC), as well as release of IFN- γ by NK cells upon contact with DCs.¹⁶¹ Additionally, Poggi and colleagues did not observe decreased killing of K562 cells by NK cells that had been treated with a CaMKII inhibitor. In this study, however, inhibition of CaMKII significantly decreased effector functions of NK cells that had been stimulated with K562 target cells. However, it

has to be taken into account that in the Poggi study specific lysis of target cells was studied, while in this thesis degranulation and the release of cytokines was analyzed. Also in this thesis, degranulation was assessed in CD3⁻CD56⁺ NK cells after 2 hours of incubation, while Poggi and colleagues analyzed CD3⁻CD16⁺ NK cells after 4 hours and used a completely different set of CaMKII inhibitors. It might therefore be possible, that CaMKII is coordinating degranulation, but not involved in other processes that might lead to killing of target cells.

Kinase inhibitor CID755673 has been described to be specific for PKD kinase family members PKD1, PKD2 and PKD3. With 200 other targets, it did not show any effect.¹⁶² It could also been shown that CID755673 has no effect on the activity of protein kinase C (PKC), usually lying upstream of PKD kinase in signaling networks, or CaMKII. This again proves high specificity of CID755673 as these kinases are closely related to PKD.^{162,163} Interestingly, PKD2 is considered as a signaling component in NK cells although functional data underlying this hypothesis are missing. However it has been shown that isoforms of PKD do not play a role in integrin-mediated lymphocyte adhesion and homing to lymphoid tissues.¹⁶⁴ In the present study, application of CID755673 led to remarkable changes in NK cells degranulation and cytokine release. These observations suggest that PKD family kinases are participating in the signal network coordinating NK cell effector functions.

4.1.2 Role of PKD and CaMKII in NK cell activation

Experiments in pure NK cell cultures also revealed inhibitory effects of the three used inhibitors in these pure cultures (3.1.2). Surprisingly, responses to inhibitor treatment in pure NK cells were different from the responses that were detected in PBMC cultures. Not only displayed the different donors remarkably variable response profiles in pure NK cells. It was also observed that used inhibitors have the capability to enhance NK cell effector functions. This observations suggest also possible roles for the analyzed kinases in inhibitory pathways. As protein kinases are part of a multitude of different signaling pathways, this is very much possible. Coordination of kinase activity and substrate binding, and therefore realization of pathway-specific functions of kinases are most likely controlled by post-translational modifications. It has already been shown that phosphorylation status of S876 directly correlates with PKD2 activity.¹⁶³ Activity of CaMKII relies on phosphorylation status of amino acid Thr286.¹⁶⁵ A study of König and colleagues could reveal additional phosphorylation sites in these kinases that had not been described before, and were not functionally described so far: engagements of NK cell receptors was shown to induce phosphorylation of PKD2 at S214 and of CaMKII at S330.¹³⁴ Although a number of different phosphorylation sites are described for both kinases, no mechanistic model exists explaining their involvement in NK cell activation.

To better understand donor variations and the apparent conflicting results generated in PBMC and pure NK cell cultures, the expression of kinase isoforms has to be considered. For example, protein kinase C isoforms (PKC δ , ϵ , θ , and η) act as upstream signal components of PKD family kinase isoforms (PKD1, PKD2, and PKD3).^{166–168} Protein kinase C isoform PKC δ has been described to phosphorylate PKD1 and PKD2, while PKC ϵ and PKC η activate PKD1.^{168–170} Unfortunately, there is no data available regarding isoforms phosphorylating PKC θ and PKD3. Importantly, PKC θ plays a pivotal role for ITAM-mediated release of IFN- γ and TNF- α , but not for NK cell-mediated cytotoxicity or cytokine release induced by IL-12 and IL-18.¹⁷¹ Interestingly, a different study reported a reduced IL-12-induced IFN- γ response of NK cells in PKC θ knock out mice (PKC $\theta^{-/-}$).¹⁷² In the same study however, a reduction of cytotoxic potential of NK cells against YAC-1 target cells could not be detected. Additionally, NK cells of PKC $\theta^{-/-}$ mice were reported to display a reduced capacity to degranulate when triggered with RMA-S tumor cells.¹⁷³ Taken together, when comparing these results with the data generated in the present work, it becomes apparent that an isoform-specific knock-out of upstream kinase PKC θ leads to a less pronounced inhibition of NK cell effector functions than chemical inhibition of PKD, a signaling component downstream of PKC. It is therefore possible, that the signaling pathway leading to NK cell activation depends not solely on PKC θ , but also involves other isoforms of PKC that phosphorylate one or more PKD isoforms (Fig. 38).

In conclusion, chemical inhibition of either CaMKII or PKD family kinases limits NK cell effector functions. Results from natural cytotoxicity further substantiated the role of these kinases in NK cell signaling. However, the results with pure NK cells also indicate the importance to further investigate the molecular basis of donor variations, which may be caused either by differential pre-activation of kinases at the level of post-translational modifications or simply by differential expression of kinase isoforms.

4.1.3 Perspectives for kinase inhibitors in cancer and NK cell therapy

In cancer therapy, the application of small molecular kinase inhibitors has been a valuable tool for years.¹⁷⁴ However, results from this study provide novel insights into the effects of donor variability and chemically-mediated NK inhibition, and its potential use.

First, this study reveals potentially dangerous side effects of kinase inhibitors. Especially dasatinib, which is already used as a tool in cancer therapy against chronic myelogenous leukemia (CML) and acute lymphoblastic leukemia (ALL)^{155,175} has drastic effects on the effector functions of NK cells (3.1.1, 3.1.2). But also CID755673, which as well inhibits NK cell activity, has already been suggested as an therapeutic drug in prostate cancer.^{162,176} Although these compounds exert anti-tumor properties, this thesis shows that their application poses

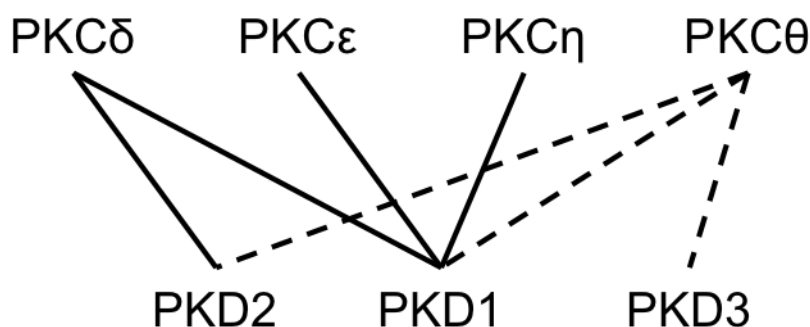


Figure 38 | Schematic representation of known and potential interactions between PKC and PKD family kinase isoforms. Continuous lines indicate known interactions between specific PKC and PKD family kinase isoforms leading to activation through phosphorylation of the latter. Potential interactions of specific PKDs with PKC θ isoforms, to this date not experimentally validated, are shown as dashed lines.

certain risks. Both compounds have in general a negative effect on the immune response against tumor cells, and might also diminish other activities from other immune cells. For dasatinib, it has also been shown that application decreases T cell activity.¹⁷⁷ Therefore, application of these compounds might lead to increased susceptibility for opportunistic infections, formation of new tumors or the original tumor itself and the capability of kinase inhibitors to modulate immune cells has to be evaluated when considering them as anti-cancer drugs. Also, during the course of this thesis it has become apparent that cells from different humans react differently to inhibitor treatment. Not only the inhibitory effect was different from donor to donor, some even reacted with increased responses. Consequently, in cancer therapy it would make sense to check the sensitivity of the patient against the applied drug before starting the treatment. This would not only help against wrong dosing of the respective drug, but also prevent over-reactions of the immune system.

Second, kinase inhibitors are a promising tool to treat diseases that are mediated by NK cell hyperactivity. However, very little is known about pathogenic conditions that are caused by NK cell activity. The number and activity of NK cell is reduced in most diseases caused by autoimmune reactions. However, some studies speculate about disease-promoting role of NK cells in these cases.^{178,179} Also, NK cells can undergo malignant transformation and actually become cancer cells. This rare type of large granular lymphocyte (LGL) can be chronic or aggressive.^{180–182} In its chronic state, therapy is relatively simple and patients have a positive prognosis. The rare aggressive form, however, is classified as one of the most aggressive tumors encountered and resistant to various therapeutic agents. Patients are left with a very poor prognosis and usually die within a few months, due to disseminated disease with associated coagulopathy and multiple organ failure. In cases like this it is logical, that

treatment with kinase inhibitors that are not only effective against leukemia, but can also diminish overly active NK cells, could help in treating this dangerous disease. However, data in actual patients or even animal models is missing.

4.2 Novel mechanisms of innate immunity in MAIT cells

4.2.1 Proteomic analysis of low-abundant primary immune cells

A challenge in the present thesis was to establish a proteomic workflow that would be suitable to comparatively analyze the proteome of small cell numbers. Screening of healthy donors had revealed MAIT cell numbers that were below 1 % of total T cell count for some donors (3.2). This resulted in amounts of sorted cells of less than $1 \cdot 10^6$ cells per buffy coat in some donors, that were then used for test experiments (Fig. 16). To cope with these possibly small cell numbers and to maximize the yield of the resulting low amounts of protein, a lysis protocol with a minimum of sample loss was chosen (see 2.7.1). The protocol is based on lysis with urea and does not contain any protein extraction steps before tryptic digest that could decrease the protein yield. With this protocol, and subsequent SCX subfractionation with a 15 minute long gradient of increasing salt concentration, it was decided to set the run length of the LC preceding the MS measurements to the maximal 120 minutes for every SCX-generated fraction. This approach made it possible to identify 2260 proteins out of 250 000 PBMCs (3.4), and it was therefor decided to keep this protocol unchanged also for the comparative MAIT cell experiments. Here, MS analyses led to the identification of 3700 to 4300 proteins per donor (Tab. 11), albeit the cell numbers varying from $1.7 \cdot 10^6$ to $9.8 \cdot 10^6$ cells per donor. This might be due to the rather short SCX gradient used. The use of a longer gradient could have led to a larger number of proteins identified. However, this workflow was highly reproducible and led to a robust modification of a large number of proteins over several experiments, and was therefor suitable for the experiments conducted during this thesis.

4.2.2 Proteomic results are in accordance with current knowledge

This study provides the first proteomic overview of the protein abundance in MAIT, NK and cCD8⁺ T cells. However, flow cytometric analyses of selected effector molecule expression in MAIT cells have been published,^{80,117} as well as a recent transcriptomic study comparing CD8⁺CD161⁺⁺ and CD8⁺CD161⁻ cells.¹⁴⁶

In 2011, flow cytometric analyses revealed multidrug resistance protein 1 (MDR1) to be prominently expressed on MAIT cells, and already reported as high, MAIT-specific expression

of CD26,⁸⁰ who has recently be suggested as a specific marker for MAIT cells.⁸² Also, low expression of CD62L in MAIT was reported, which is consistent with their classification as effector cells. These observations could be repeated in this study (3.5.3.2, Tab. 14), showing the reliability of the generated data. The same study also summarized cytokine secretion profiles of MAIT cells after stimulation. However, none of these secreted cytokines, e.g. IL-17 or IFN- γ , could be identified in the proteomic data set. Granzyme B (GzmB) was reported to be released in same amounts by MAIT and cCD8⁺ T cells after stimulation with PMA/ionomycin and CD3/CD28 antibody stimulation, respectively. Accordingly, proteomic data showed abundance of GzmB in MAIT and cCD8⁺ T cells to be equal (3.5.4.1, Tab. 15).

A recent study by Kurioka and colleagues focused on quantification of granzyme expression in MAIT cells by flow cytometry.¹¹⁷ Granzyme A (GzmA) and granzyme K (GzmK) were identified to be highly expressed in MAIT cells. This could be confirmed by proteomic analysis (3.5.4.1, Tab. 15), with log₂RF MAIT:cCD8⁺ of 1.60 and 1.91 for GzmA and GzmK, respectively. In the Kurioka study, however, expression levels of pore-forming protein perforin, granulysin and GzmB were reported to be lower in resting MAIT cells than in cCD8⁺ T cells, whereas previous studies have shown them to be secreted in prominent amounts upon stimulation.^{80,94} Also, proteomic data showed perforin, granulysin and GzmB to be present in equal amounts in MAIT and cCD8⁺ T cells (3.5.3.2, 3.5.4.1, Tab. 14 & 15). Furthermore, flow cytometric data showed that only 20 % of all CD8⁺ T cells are positive for GzmB, all of them defined as conventional CD8⁺ T cells due to their low or intermediate expression of CD161. Also, only 25 % of the CD8⁺CD161⁻/CD161⁺ T cells were positive for perforin, while 10 % of CD8⁺CD161⁺⁺ MAIT cells were detected to express perforin. Only 10 % of non-MAIT CD8⁺ T cells were positive for granulysin.¹¹⁷ Thus, the difference between antibody based detection that indicated lower GzmB, perforin and granulysin expression in MAITs, and proteomic analysis which could not detect any difference, might be due to the fact that indeed only a small set of cCD8⁺ T cells expresses these proteins.

Also in 2014, an extensive study was published, where the authors systematical analyzed the difference between CD8⁺CD161⁺⁺ and CD8⁺CD161⁻ T cells on the level of mRNA.¹⁴⁶ As almost all CD8⁺CD161⁺⁺ T cells are MAIT cells in the transcriptomic study, and the majority of MAIT cells is CD8⁺ in the proteome analysis, this study can be compared with the proteomic analysis. Interestingly, only a relatively small amount of regulated genes or corresponding proteins overlapped in both studies, although no extreme differences in terms of regulation factors were present (3.5.3.2, Tab. 13). No downregulated gene was to be found upregulated as protein and vice versa. Among the genes and proteins that were consistently identified as regulated in both studies is effector molecule GzmA. The transcriptomic analysis, however, identified 544 regulated genes. Out of those, 384 of the regulated genes weren't identified on

the the protein level at all. Out of the overlapping 160 proteins, 141 genes were identified as regulated that were not found to be regulated on the protein level. Also, by coincidence the same number, 141 proteins that were found to be regulated were described as not regulated by the transcriptomic data. This discrepancy might be explained by the stringent conditions applied to identify regulated proteins in the proteomic set. It might also be a result of post-translational regulations of protein levels, that would lead to a different protein abundance as the one that was indicated by the mRNA amounts. Finally, the compared cell subsets are not identical with the ones in the present study, which might also lead to falsification of results. Interestingly, transcriptomic comparison of CD8⁺CD161⁺⁺ and CD8⁺CD161⁻ T cells also did not detect different expression of GzmB, perforin or granulysin,¹⁴⁶ although the compared cell types were completely identical to the ones used in the Kurioka study in which different expression levels of these proteins could be detected.¹¹⁷

Taken together, flow cytometric studies mostly reflect the regulation that was determined by mass spectrometry, and also identify GzmA and GzmK as key proteins for MAIT cell effector functions, with increased abundance when compared with conventional cytotoxic T cells. The comparison with transcriptomic data however requires further careful validation, although now major contrasts could be detected.

4.2.3 Is the definition of a “typical” MAIT cell possible with proteomics?

Studies with material from human donors are always subjected to the individual geno- and phenotype of humans. Therefor, it had to be ruled out that individual variations would influence the outcome of the study, and donor variability had to be taken into account.

Labeling with iTRAQ reagent and detection of the intensities of the different markers allowed to quantify protein abundance in the different donors (3.5.3.2). The difference in abundance between the three investigated cell types can be displayed as regulation factors (RF), that are equal to the fold change of abundance. Alternatively, the logarithm to the base of 2 of the fold change (\log_2 RF) can be used. This ensues in a \log_2 RF of 0 for proteins with the same abundance. A \log_2 RF value of 1 indicates a two-fold abundance increase, while \log_2 RF -1 shows that the respective protein is half as abundant in one cell type when being compared to the reference. When investigating the distribution of \log_2 RF it became apparent, that almost all donors showed a similar general distribution of values (Fig. 30). Additionally data also demonstrated regulation factors for every single protein that were more or less coherent over every donor (Fig. 31). Donor 2, however, is an exception from the else consistently looking data. The regulation factors of donor 2 are spread significantly further than the \log_2 RFs of the other four donors (Fig. 30). Also, donor 2 showed a different pattern of distribution of the \log_2 RF, which can be seen in Fig 31. Yet, this donor-dependent

variation is nothing out of the ordinary. Primary cells are known for showing donor-dependent variations, and were also observed to display huge differences in percentages of the different cell types (3.5.1, Tab. 10). Similar observations about human donors showed large variation of immune cell responses to infection, again indicating the variability of primary material.¹⁸³ Additionally, in the part of this thesis analyzing NK effector functions donors showed variation when reacting to treatment with kinase inhibitors (3.1.2, Fig. 14). Also in proteomic studies, similar donor variations could be observed.^{19, 184} The reason for donor 2 to show this distinct distribution of regulation factors remains open to speculation. Donor 2 was a 36-year old healthy male and had the largest number of MAIT cells. The number of initially isolated PBMCs was high, but not abnormally increased (data not shown). Also with regard to lymphocyte numbers, or percentages of T cells and MAIT cells no significant deviation of a single factor was detected (data not shown). However, all these factors in combination finally resulted in a total of almost $10 \cdot 10^6$ MAIT cells isolated. Although this donor was also classified as healthy and tested negatively for HIV, HBV and HCV, it can of course not be excluded that he suffered or recovered from a not-detected infection. Nonetheless, infections and even auto-inflammatory diseases are usually accompanied by a decrease of MAIT cell numbers in peripheral blood.^{77, 113, 115, 125, 128, 129, 131} The increased number of MAIT cells might have been an effect of overcompensation when restoring their numbers after an recently-cleared infection. It is then also possible, that the amount of stronger or differently regulated protein might then be due to this infection, that had not be detected. It might be imaginable that cells acquire a more diverse proteomic phenotype when exerting their different effector functions during and after the course of an infection. If this is the case, it opens up the possibility to use MAIT cell numbers as a marker for disease progression.

However, as donor 2 was, with respect to the data available, completely healthy and did not show any anomalies in cell numbers or percentages, it was decided to keep the data as unbiased as possible and not remove the donor from the analysis. Interestingly, it was nevertheless possible to define a large number of proteins that were regulated in all five donors, revealing sets of proteins that are indeed regulated donor-independently in MAIT cells, and therefore define the typical MAIT cell.

4.2.4 Best of both worlds: Typical MAIT cells between NK cells and CD8 T cells

As MAIT cells are usually described to be “innate-like T cells”, an aim of this thesis was to assess how “innate-like” MAIT cells actually are. The study was therefore designed to compare MAIT cells with both adaptive and innate immune cells, in this case conventional

CD8-positive T cells, that are not MAITs (cCD8⁺ T cells), and NK cells, respectively. It is an advantage of systematic analyses containing quantitative data, that these kind of data usually allow general statistical comparison of different analytes, in this case cell types.

Statistical analyses like principal component analysis or multidimensional scaling make it possible to visualize the level of similarity of individual cases of a dataset. It was therefore tried to calculate the similarity or distance between MAITs, NK cells and cCD8⁺ T cells. Available data however, did not lead to satisfying results, as it was not possible to normalize quantitative data sufficiently. This approach resulted in a clustering of the different experiments rather than in clustering of different cell types (MAITs, NK, cCD8⁺, data not shown). This indicates that the technical variance of mass spectrometry makes it difficult to impossible to compare different experiments with systematic approaches, even with various methods of normalization applied. This leaves the number of proteins regulated between the cell types as a method to assess the similarity between different cells. In five donors, 135 proteins were identified with significantly different regulation factors between MAIT and NK cells (see 3.5.3.2, Tab. 12). When comparing MAIT and cCD8⁺ T cells, 160 proteins were significantly regulated while the number of regulated proteins between NK and cCD8⁺ T cells was 231. When assuming that cell types are more different if more proteins are differentially express, these numbers might indeed give a rough estimate about how similar the cell types are. Numbers then indicate that NK and cCD8⁺ T cells are the most different. Surprisingly, the difference between innate NK cells and MAIT cells would then be lower than the difference between MAIT and adaptive cCD8⁺ T cells. This would indeed indicate a more innate-like phenotype of MAIT cells, which would then be phenotypically located between NK and cCD8⁺ T cells, with displaying surprising phenotypical similarity to NK cells (Fig. 39).

4.2.5 Defining the typical MAIT cell phenotype with proteomics

4.2.5.1 A new set of markers for human MAIT cells

MAIT cells are usually defined as T cells, that express the invariant V α 7.2 TCR chain, and high amounts of CD161.⁹⁴ Recently, also other markers for MAIT cells have emerged, like IL-18 receptor,⁸⁰ MDR-1⁸⁰ or CD26.⁸² However, distinct intracellular marker is missing. Proteomic data also could identify a number of proteins, that are exclusive for MAIT cells (Tab. 18) and can serve as distinct MAIT markers. Importantly, this list also includes CD26 as the highest regulated protein between MAIT and cCD8 T cells, and can serve as a proof for the validity of the identified markers. Interestingly, among this putative marker molecules are also surface markers that have never been described in the context of MAIT cells before. CD98 transporter for large amino acids, like tryptophane,¹⁸⁵ and CD48 is a activation marker for B cells and the

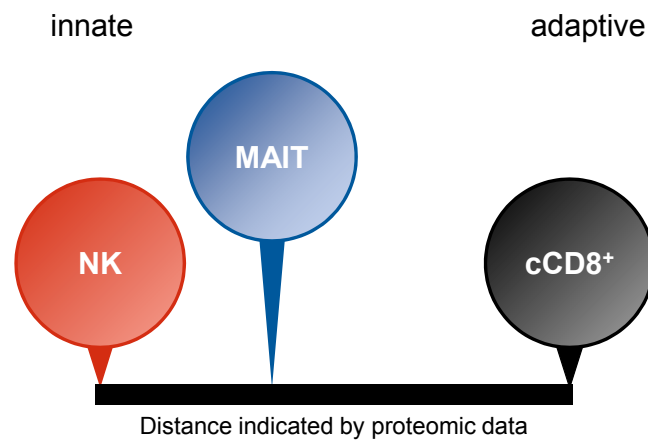


Figure 39 | Similarity between human NK, MAIT and cCD8⁺ T cells. Proteomic data indicated a more similar phenotype of MAIT cells to NK cells than to cCD8⁺ T cells, as less proteins were found to be significantly regulated between MAIT and NK cells as between MAIT and cCD8⁺ T cells.

ligand for CD2.¹⁸⁶ Both of these molecules could be confirmed to be increased on MAIT cells in the course of this study (3.5.3.3, Fig. 32). Intracellular markers for T cell subpopulations are usually transcription factors, like FoxP3 for regulatory T cells. However, these are often low abundant and detection is therefore difficult. For example, typical MAIT cell transcription factors like ROR γ t or PLZF could not be identified in this highly sensitive proteomic approach. Intracellular proteins like L-amino-acid oxidase or secernin-1 however, were found to be highly abundant, and can therefore serve as marker for MAIT cells.

4.2.5.2 The arsenal of MAIT cells - innate immunity requires a specific pattern of effector molecules

MAIT cells have already been subject to investigations aiming to define their exact effector function and also the effector molecules that allow them to exert these functions. However, proteomic studies allow the systematic identification of differentially regulated proteins, and generated data are furthermore not restricted to molecules that are detectable by antibodies like in Western Blot or flow cytometric applications. Additionally, with an unbiased method like mass spectrometry, it is not necessary to decide what proteins would be of interest before conducting experiments. It was therefore possible, to identify effector molecules that are typical for MAIT cells, when compared with NK and conventional, CD8-positive T cells (cCD8⁺ T cells), respectively (3.5.4.1, Tab. 15). Among these were all human granzymes, important effector molecules in immunity.^{64, 187–189} All known granzymes are serine proteases and usually associated with the induction of target cell death.

Granzyme A (GzmA) showed a similar abundance in MAIT and NK cells, and was found to be less abundant in cCD8⁺ T cells. It has been shown to be expressed in higher levels in MAIT cells, and colocalizes with granzyme K and CD107a.¹¹⁷ Current knowledge implicates that GzmA uses a different, caspase-independent pathway than other granzymes to induce apoptosis. It has been shown that GzmA enters the matrix of mitochondria and mediates the generation of mitochondrial super oxide, dissipating the membrane potential.¹⁹⁰ Additionally, oxidative stress leads to relocalization of the redox-sensitive SET complex to the nucleus, where GzmA can enter, liberating nucleases and in this way inducing DNA damage.^{191,192} Interestingly, the cytotoxic potential of human GzmA is lower than the one of murine GzmA,¹⁹³ and the efficiency of hGzmA to induce cell death has been discussed. Instead, extracellular GzmA has been shown to trigger the release of IL-1 β , TNF- α , IL-6 and IL-8 in human monocytes,^{194,195} and of IL-6 and IL-8 of fibroblast and epithelial cell lines.¹⁹⁶ Furthermore, GzmA multiplies the lipopolysaccharide (LPS)-induced cytokine release by human monocytes.¹⁹⁷ Also, GzmA-release by $\gamma\delta$ T cells induces TNF- α secretion in human macrophages infected by mycobacteria, thereby inhibiting the growth of the microorganisms.¹⁹⁸

Granzyme B (GzmB) was detected with the highest abundance in NK cells, with MAITs and cCD8⁺ T cells showing significantly lower abundance. Until now, GzmB has been described to be not expressed at all in MAIT cells¹¹⁷ and rapidly induces apoptosis, usually using a mechanism that is dependent on caspases.¹⁹⁹ As all members of the granzyme family, GzmB also exerts proteolytic functions and is able to cleave its target proteins after aspartic acid residues.²⁰⁰ It can for example cleave caspase 3,²⁰¹ which however doesn't result in its full activation.^{202,203} Additionally, GzmB also shows strong preference to proteolytically activate Bcl-2 family member Bid,²⁰² initiating the relocalization of Bid to the mitochondria and subsequent permeabilization of the outer membrane. This leads to the release of mitochondrial intermembrane molecule Smac/Diablo and cytochrome C.²⁰³ The interactions of the latter with Apaf-1 facilitate apoptosome formation and activation of caspase 9, while Smac/Diablo relieves inhibition of caspase 3 activity by inhibitor of apoptosis protein 3 (IAP3). All these processes allow caspase 3 to become fully active and effectively induce target cell apoptosis. Apart from its cytotoxic capacity, GzmB has also been shown to synergistically increase the secretion of TNF- α from primary human monocytes, similar to effects of GzmA or GzmK.¹⁹⁷ Also, GzmB is able to process cytokines, like pro-IL18 or the precursor of IL-1 α , enhancing increasing its biological activity.

Granzyme H (GzmH) was found to be higher abundant in NK cells than in cCD8⁺ T cells, and displayed the lowest abundance in MAIT cells. The precise mechanism of GzmH-mediated apoptosis is still under debate, and pathways independent²⁰⁴ and dependent,²⁰⁵ respectively, of cleavage of Bid, ICAD (inhibitor of caspase-activated DNase)/DFF45 (DNA Fragmentation

Factor 45) and caspase-3 have been suggested for GzmH-mediated apoptosis. The most recent work on GzmH functionality suggest that the enzyme indeed cleaves and activates DFF45, but is independent of Bid activation.²⁰⁶ Nevertheless, GzmH disrupts the outer mitochondrial membrane and releases cytochrome C and Smac/Diablo, much like GzmB. The neutralization of IAPs and the generation of an apoptosome, however, are not required to induce GzmH-mediated cell death. No immune-modulatory functions of GzmH have been described so far. There is however evidence for anti-viral functions of GzmH, as it can proteolytically inactivate virus-derived inhibitors of GzmB²⁰⁷ or different viral proteins.²⁰⁸

Granzyme K's (GzmK) increased abundance in MAIT cells in comparison with both NK and cCD8⁺ T cells has already been suggested by flow cytometric data.¹¹⁷ Granzymes A and K are closely related,¹⁹² and similar to GzmA, GzmK also cleaves the SET complex, leading to apoptotic processes.²⁰⁹ It has also been reported, that GzmK can cleave p53 to proapoptotic forms, indicating a unique mechanism for GzmK-mediated killing.²¹⁰ However, also the killing efficiency of GzmK has been questioned, and other functions were suggested. Similar to GzmA, GzmK can trigger the secretion of IL-6 and IL-8 from human fibroblasts.²¹¹ Strikingly, GzmK can also interact with bacteria and LPS, and in combination with LPS increases the release of TNF- α , IL-6 and IL-8 *in vivo* and *in vitro*.¹⁹⁷ Furthermore, GzmK has been shown to cleave β -tubulin.²¹²

Granzyme M (GzmM) showed the lowest abundance in cCD8⁺ T cells, and the highest in NK cells. It has been described that GzmM is highly expressed in NK and NKT cells, and expressed in a third of all CD8⁺ T cells.²¹³ It was therefore been attributed a role in innate immunity,²¹⁴ although more recent studies have revealed high expression of GzmM in differentiated effector T cells.²¹⁵ Interestingly, GzmM could also be detected in cCD8⁺ T cells in this thesis, and showed significantly higher abundance in MAIT cells. The function of GzmM however and physiological relevance, is not yet completely understood, also because of contradictory data.²¹⁶ Different mechanisms about GzmM inducing cell death have been reported. One study characterized the cell death induced by GzmM as accompanied by chromatin condensation and rapid lysis, but not cytochrome C release, caspase 3-activation, loss of membrane potential or DNA fragmentation.²¹⁷ Different studies have shown that GzmM indeed does lead to DNA fragmentation, mitochondrial damage and caspase activation.^{218,219} The differences in result may be due to varying experimental procedures as it has been suggested by de Poot and Bovenschen.²¹⁶ Additionally, GzmM has been shown to cleave α -tubulin, thereby destabilizing the microtubule network of the cell.²²⁰ There is also data available for human GzmM to promote inflammatory processes. Nevertheless, in mice it could be shown that also mGzmM seems to synergistically enhance the inflammatory response to LPS challenging,²²¹ and furthermore promotes secretion of macrophage inflammatory

protein-1 alpha (MIP-1 α) from NK cells.²²²

Granulysin could be detected with the highest abundance in NK cells, with MAIT and cCD8⁺ T cell showing a lower similar abundance. Granulysin is a cytotoxic protein^{65,223} that is usually expressed in NK cells and T cells.²²⁴ Granulysin is synthesized as a molecule of 15 kDa, and later cleaved into a 9 kDa form.²²⁵ While the 15 kDa form is secreted constitutively, the 9 kDa form is located in cytolytic granules and shows antimicrobial and tumoricidal activity if recombinantly expressed.²²⁴ The 9 kDa form of granulysin can bind to the membrane of the target cell and breach it, thereby entering the cell and causing calcium influx.^{226,227} This also leads to subsequent decrease of intracellular potassium, all this causing mitochondrial damage, releasing cytochrome c and apoptosis-inducing factor into the cytoplasm, triggering a caspase-dependent mechanism that leads to apoptosis.²²⁸ Interestingly it has also recently been shown that granulysin also plays a vital role in the direct killing of mycobacteria by NK cells.²²⁹

Perforin was found to be extremely high expressed in NK cells, and in similar amounts in MAIT and cCD8⁺ T cells (Tab. 14). Perforin is a pore-forming protein, that plays a pivotal role of delivering granzymes into the target cell cytoplasm.^{63,230,231} Its function is absolutely vital for the immune system, humans and mice that suffer from perforin-deficiency have to deal with increased susceptibility to infections or cancer.^{232,233} The exact mechanism of perforin to deliver granzymes into the target cell is not completely understood.²³⁴ Two models have been suggested, one proposing that perforin forms pores in the plasma membrane, through which the granzymes are delivered.²³⁵ More recent studies however indicate a two-step process, where first indeed pores in the plasma membrane are formed through which the granules enter. Subsequently, perforin also forms pores in the membrane of endocytosed endosomes, releasing the cytotoxic granzymes into the cytosol.²³⁶

Interestingly, quantification of effector molecules revealed a pattern of expression that is typical for MAIT cells, not only when being compared with NK cells. Also, MAIT cells express a profile of granzymes that is distinct from cCD8⁺ T cells (Fig. 40). While the differential expression of perforin, granulysin, GzmA, GzmB and GzmB in MAIT and cCD8⁺ T cells has already been discussed on the base of flow cytometric analysis by Kurioka and colleagues,¹¹⁷ new data in this study indicate also a specific expression pattern for GzmH and GzmM. Apart from that, proteomic data clearly indicates that NK cells express the most complete granzyme panel when being compared with the other investigated cell types, with high amounts of GzmB, granulysin and perforin, which all exert pronounced cytolytic activity. The only exception is GzmK that is abundant in lesser amounts than in MAIT cells, which show the highest abundance of all cell types. Previous studies have also described GzmK as highly prevalent in MAIT cells,¹¹⁷ so proteomic data further underlines a possible pivotal

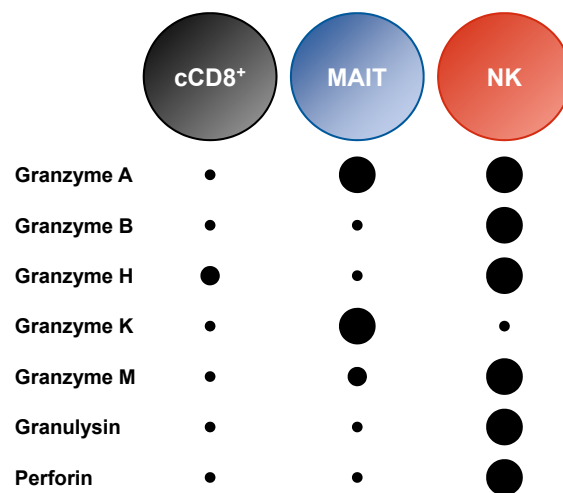


Figure 40 | Differential abundance of effector molecules in cCD8⁺ T, MAIT and NK cells. Relative protein abundance of effector molecules in the different cell types was determined by mass spectrometry (3.5.4.1, Tab. 15), and is display schematically. The circle size displays the relative regulation for the respective protein, with increased and decreased size pointing out increased and decreased abundance, respectively. Circles of the same size indicate no regulation. NK cells possess an almost complete arsenal of granzymes when compared with the other cell types, with the exception of GzmK, which is highly upregulated in MAIT cells. MAIT cells also express GzmA in high amounts, while cCD8⁺ T cells express the lowest amounts of effector molecules.

role of GzmK in the MAIT phenotype. MAIT cells also express GzmA and GzmM in high and intermediate amounts, respectively. Interestingly, cCD8⁺ T cells show the lowest abundance of all effector proteins when compared with the other cell types, with the exception of GzmH that is higher expressed than in MAIT cells. abundance of GzmM has never been described in MAIT cells before, and interestingly also showed an increased expression when compared with cCD8⁺ T cells, indicating a more pronounced role of this effector molecule in MAIT cells than in cCD8⁺ T cells.

Also based on proteomic data, the effector phenotype of resting MAIT cells is dominated by GzmA and GzmK (Fig. 40), which have recently emerged as exerting rather pro-inflammatory than cytotoxic functions.^{194–196} Strikingly, both proteins have also been shown to specifically interact with LPS and target intracellular bacteria,¹⁹⁷ which is in accordance with the anti-bacterial functions of MAIT cells. The high abundance of GzmM also discriminates MAIT from other cytotoxic T cells, and has not been discussed before. Also GzmM is only mildly cytotoxic, but also shows LPS-dependent proinflammatory potential in mice.²²¹ Interestingly, abundance of GzmM increases during T cell differentiation from naïve to effector T cells,²¹⁵ indicating the phenotype of MAIT cells that resembles the one of antigen-experienced CD8⁺ T cells. GzmH was the only granzyme significantly downregulated in MAIT cells, but its

pro-apoptotic and anti-viral functions are still under debate. In summary, the granzyme expression profile of resting MAITs indicate a more pro-inflammatory than cytotoxic phenotype when compared with conventional cCD8⁺ T cells, with higher expression of granzymes A, M and K. Interestingly, all these granzymes have been shown to exert specific, anti-bacterial functions which are in accordance with the anti-bacterial phenotype of MAIT cells. It also shows, that MAIT cells can react quicker than conventional T cells, as they already have a panel of granzymes ready to secrete. However, the dedicated pro-inflammatory function of these highly abundant proteins can potentially lead to problems if MAIT cells contribute to auto-immune inflammations, a problem that has been discussed already.²³⁷ Their role in auto-immune diseases like inflammatory bowel disease is not yet clear, and it might be that their ability to infiltrate the sites of inflammation and their high amounts of pro-inflammatory cytokines and granzymes might influence the course of the inflammatory response negatively. This, together with the rather unspecific type of antigen MAITs recognize leads to the question on how tightly MAIT activity is actually regulated. This has especially to be considered in the gut, where the commensal flora is very much present and can produce MR1 ligands that can lead to MAIT activation, and potentially lead to excessive reactions and cytokine release. In contrast to NK cells, however, resting MAITs express less cytotoxic proteins, with decreased abundance of perforin, granulysin and the highly cytotoxic granzyme B. When triggered, MAITs cells rapidly start expressing these proteins,^{80,117} rendering them able to lyse target cells even more efficiently. So the way to prevent MAIT cell over-activation in the first hours of infection might be the low abundance of cytotoxic granzyme B in resting cells and the general low responsiveness to TCR-dependent stimulation.^{76,80,85} Later, when MAIT cells are highly cytotoxic, stimuli independent from TCR-signaling and therefore cell-to-cell contacts become even more important.¹¹⁰ All these factors might hinder MAIT cells from reacting excessively to stimuli provided to their rather unspecific TCR, and cause damage through cytotoxic effectors.

4.2.5.3 Increased capacity for exocytosis in typical human MAIT cells

In general, MAIT cells are considered part of the innate, or innate-like immune response. As innate immune cells are almost the first line of defense against pathogens, they have to react quickly. In the proteomic data, evidence was found that indeed MAIT cells possess the capability for a quicker, more pronounced exocytotic response.

A significantly regulated protein was LFA-1. Expression of LFA-1 is increased on effector T cells, and rises the affinity of T cells for target cells.⁵⁵ Accordingly, proteomic data revealed MAIT cells to show mildly increased expression of LFA-1 (log₂ RF MAIT:cCD8⁺ 0.63, regulated in three of five donors), which again substantiates the fact that MAIT cells have an effector

phenotype.

Systematic analysis of significantly upregulated pathways with MetaCore GeneGo showed that the most upregulated pathways can be associated with exocytosis and secretion (3.5.4.2, Fig. 33). Furthermore, closer analysis of the upregulated single proteins (Tab. 16), that are part of these pathways revealed that all of them are indeed rather promoting exocytosis or processes associated with immunological synapse formation, like cytoskeletal remodeling. Most of them are increased similarly in MAIT and NK cells, when being compared with conventional CD8⁺ T cells.

Alpha-actinin 4 is a non-muscular isoform of alpha-actinin, like alpha-actinin 1.²³⁸ Accordingly, only these two members of the alpha-actinin family were identified in the MAIT proteome. The alpha-actinin family is in general associated with linking actin filaments to the plasma membrane, and cytoskeletal remodeling^{148,239} which is a vital part in immune cell polarization and activation. Also, the ability of alpha-actinin 4 to bind actin is dependent on calcium,²⁴⁰ whose influx upon T cell activation plays a vital part in triggering T cell effector functions. Interestingly, isoform alpha actinin 1, which has high structural and sequential homology, has been shown to link LFA-1 to the actin cytoskeleton.²⁴¹

Annexin IV is a calcium-dependent phospholipid binding protein, that has been suggested to play a role in synaptic exocytosis as it is located on synaptic membranes and forms a complex with rabphilin and synaptotagmin 1.¹⁴⁹ Also, annexin IV localizes towards the membrane after calcium influx.²⁴²

Unconventional myosin-1f is closely related to actin motor protein myosin 1 and highly expressed in immune cells. Knowledge about its specific function is very fragmentary. However, like all myosins, isoform 1f also possesses a motor domain,²⁴³ and might therefore be also implicated in transport towards the immunological synapse like other myosin class I isoforms.¹⁵⁰

Synaptotagmin-like protein 2 (Slp2) has already been shown to interact with Rab27a in cytotoxic lymphocytes, localizes at the immunological synapse and significantly contributes to secretory lysosome exocytosis from CTL.¹⁵¹ It has also reported that Slp2 is responsible for inducing polarity in epithelial cells.²⁴⁴

Secernin-1 is especially interesting, as it is not only upregulated when compared with cCD8⁺ T cells, like the others, but also when compared with NK cells (Tab. 16). Therefore, it might be vital for MAIT cell function. Secernin-1 has been shown to promote exocytosis in mast cells in a calcium-dependent manner,¹⁴⁷ and could also realize the same function in MAIT cells. If it does, then the pronounced abundance of secernin-1 could further substantiate the fact that exocytosis is positively regulated in MAIT cells. This is further underlined by the fact that among the top twenty proteins positively regulated between MAIT and cCD8⁺ cells,

five are directly associated with exocytotic processes (Tab. 17). Among those are the already described myosin-1f, secernin-1 and alpha-actinin 4.

But also *S100A4*, a calcium binding protein, that is highly expressed in cytotoxic CD56^{dim} NK cells¹⁹ is highly abundant in MAIT cells. In NK cells it locates to the immunological synapse¹⁹ and has a role in coordinating granule exocytosis in NK cells (M. Heyner, in preparation). Annexin 1 binds phospholipids in the presence of calcium, and assemblies at the membrane.²⁴⁵ T cells that are deficient of annexin 1 show decreased activation..²⁴⁶ Numerous of these proteins are also present in the list of proteins whose expression is upregulated in MAIT cells, when compared to both NK cells and cCD8⁺ T cells, and are therefore typical for MAIT cells (Tab. 18).

Taken together, several proteins that are associated with the positive regulation of exocytosis or immune cell activation show high abundance in MAIT cells, and are typical for the MAIT cell phenotype. However, due to the heterogeneity of the exact functions of these proteins, the implications of their upregulation are not obvious. One possibility would be that exocytosis in MAIT cell is differently regulated and executed than in NK and cCD8⁺ T cells. When taking into account that MAIT cells display an innate-like phenotype and are therefore part of one of the first lines of defense against microorganisms, it is possible that they need to release their granules quicker and in larger amounts. Increased abundance of proteins like secernin-1, myosin-1f or Spl2 would enable them to do so, if their unresponsiveness towards TCR-dependent stimuli is overcome.

4.2.5.4 Controlling the killer: MAIT cells display a unique set of proteins that regulate proliferation

One of the most interesting questions in MAIT cell research is how their activity is controlled. MAIT cells react against a broad range of bacteria, of which some are part of the commensal flora.^{79,94} How their activity is controlled or regulated is so far unknown. Although MAIT cells proliferate upon activation, they display an exhausted phenotype in chronic infections, together with decreased numbers. It is possible that this is one method to prevent over-activation and autoimmunity. What mechanisms exactly control these processes however, is so far unknown.

Among the proteins typical for MAIT cells were molecules that are associated with the regulation of proliferation. It has already been reported that MAIT cells are prone to apoptosis through elevated levels of caspases-3 and -7,²⁴⁷ which might be a method to regulated their pro-inflammatory function. Accordingly it was suggested that MAIT cells die in chronic HIV infection, due to activation induced cell death.¹²⁹ Proteomic data showed that proteins L-amino-acid oxidase, galectin-3 and both parts of the CD98 heterodimer are upregulated in

MAIT cells (Tab. 18).

L-amino-acid oxidase (LAAO) is encoded by the IL-4-induced gene 1 (IL4I1) and has been shown to be highly expressed in Th17 cells and even higher in CD4⁺CD161⁺ T cells.²⁴⁸ There, it was also reported that its expression decreases IL-2 production and proliferation, and knock-down of IL4I1-mRNA accordingly increased the proliferative capacity. Additionally, its expression is controlled by transcription factor ROR γ t.²⁴⁸ In a different study, it was observed that high expression of IL4I1 leads to increased abundance of protein Tob1, that directly inhibits proliferation.²⁴⁹ In MAIT cells, the pronounced abundance of this protein has not been discussed yet. However, it is logical that the high expression of ROR γ t in MAIT cells would also result in high expression of LAAO. Also in MAIT cells, this protein will most likely inhibit proliferation, and lead to a similar phenotype as in Th17 cells.

Galectin-3 is usually present in the cytoplasm but can be secreted.²⁵⁰ Interestingly, intracellular galectin-3 prevents apoptosis, while extracellular galectin-3 can induce cell death specifically in T cells.²⁵¹ Although the concentration needed for apoptosis induction is relatively high, it has been suggested that galectin-3 might increase its apoptotic capacity when expressed on the cell surface, similar to galectin-1.²⁵² Proteomic studies revealed high abundance of galectin-3 in MAIT cells for the first time. However, the localization could not be determined. It is possible that galectin-3 is relocated to the surface after certain stimuli or activation and there induces cell death in either target cells, or even other MAIT cells. The latter might be another method of a negative feedback mechanism to regulate MAIT cell activity *in vivo*. Nevertheless, the functions of galectin-3 are diverse,²⁵⁰ so there also can be functions that are realized by this protein in MAIT cells.

CD98, or LAT1, is a heterodimer, that forms a transporter for large amino acids, like tryptophane.¹⁸⁵ It has been reported that CD98 plays an important role in activated T cells by catalyzing the influx of amino acids that serve as nutrients.²⁵³ Such high abundance of CD98 on MAIT cells implicates a state of readiness, that makes instant influx of nutrients possible, if needed. The possibility to react quickly makes sense for an innate-like cell type, and goes hand in hand with the observed upregulation of exocytotic pathways. Furthermore, a recent study has associated defects in the tryptophane metabolism in HIV patients with the depletion of MAIT cells.²⁵⁴ Authors observed a negative correlation of MAIT cell numbers and the amount of tryptophane in patient blood. However, they did not state if the loss of MAIT cells caused the depletion of tryptophane, or vice versa. Proteomic data suggest an increased need for tryptophane in MAIT cells, especially under the stress of a chronic HIV infection. This might result in a vicious circle, where activated MAIT cells use up the present tryptophane quickly, and start to die due to lack of nutrients afterwards.

Overall, MAIT cells showed unique expression of proteins associated with proliferation

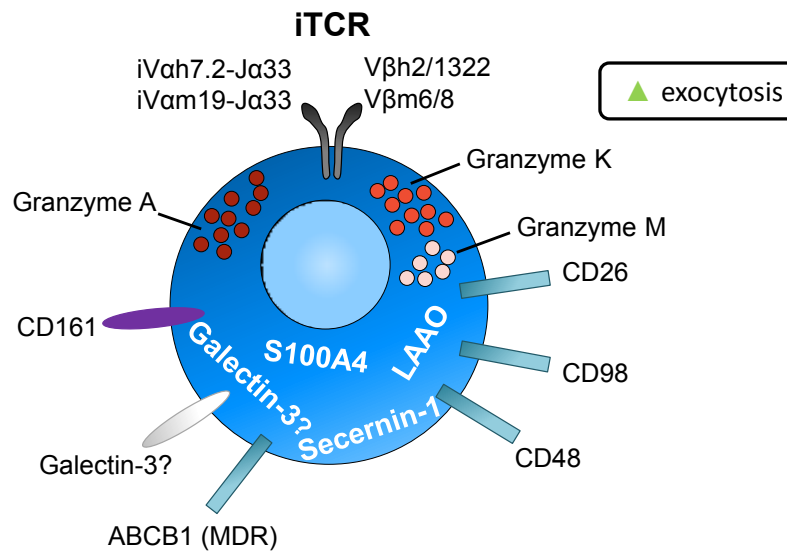


Figure 41 | Proteomic definition of a typical primary human MAIT cell. In this study, the proteome primary human MAIT cells was analyzed for the first time. Data revealed a strong upregulation of proteins associated with exocytosis, like secernin-1. High abundance of Granzymes A, K and M suggests a more pro-inflammatory than cytotoxic phenotype of resting MAIT cells. The regulation and control of proliferation seems to be controlled differently as in conventional CD8⁺ T cells, as proteins like L-amino-acid oxidase (LAAO) or CD98 showed an increased presence. Also, makers like CD48 were found to be upregulated and can be used to distinguish MAIT cells from conventional T cells. Galectin-3 has been found to be highly abundant as well, but so far it is not clear if it is located on the surface or intracellular.

and apoptosis, that differentiate their phenotype even further from conventional CD8⁺ T cells. These factors can influence the proliferation of MAIT cells themselves, but also of other surrounding cells and might therefore be a method to regulate MAIT cell activity and prevent auto-immune responses. Furthermore, high abundance of transporters for amino acids might also add to their capability to react quickly upon activation.

In total, this unique proteomic profiles underlines the uniqueness and complexity of MAIT cells, and further underline that they indeed are fundamentally different from conventional cCD8⁺ T cells (Fig. 41). A number of proteins are highly upregulated, that don't play an important role in cCD8⁺ T cells (like Granzyme M) or have never been described in that context (secernin-1, S100A4).

4.2.6 First insights into the molecular mechanisms of MAIT cytotoxicity

Although MAIT cells are functionally described, molecular mechanisms coordinating their effector functions are currently unknown. Also, the interface between MAIT cell and target

cell has never been shown before.

This study presents the first glimpse on the formation of the MAIT immunological synapse (3.6). After activation of primary human MAIT cells with monocytic cell line THP-1 that were fed with bacteria, MAIT cells showed typical polarization and localization of granules towards the interface between MAIT cell and target cell (Fig. 34). This process is typical for T cells or lymphocytes in general.^{45,57,58} Additionally, localization of the microtubule-organizing center towards the IS could be observed (Fig. 36), which is also a common process during IS formation.^{45,57,58} These first data suggest formation of a synapse, that is not too different from the one of conventional CD8⁺ T cells.

Proteomic data had also revealed increased abundance of calcium-binding protein S100A4 in MAIT cells (Tab. 15). In previous work from our group it could be shown that S100A4 is not only highly expressed in the cytotoxic CD56^{dim} NK cells subset and localizes at the NK cell IS,¹⁹ but also coordinates the directed release of cytolytic granules in NK cells (Heyner M., in preparation). Additionally, S100A4 has been suggested to colocalize with microtubuli in antibody-stimulated primary human T cells (N. Amsberg, personal communication). In MAIT cells, no direct colocalization of S100A4 and microtubules could be observed (Fig. 35). Nevertheless, in immunofluorescent pictures, structures formed by microtubuli and S100A4 became apparent, and close associations of the two proteins. As the closely related S100 proteins have been reported to interact with microtubules already,^{255,256} it is possible that it is a simple interaction that is observed here, and that could not be detected as colocalization, possibly due to sterical hindering of the used antibodies. However, these pictures nevertheless show that highly upregulated S100A4 is a structural component in MAIT cells, and might have a pivotal role in organizing the cytoskeleton.

Furthermore, in activated MAIT cells, overlap of both S100A4 and microtubules was still visible (Fig. 36). Interestingly, S100A4 also localized towards the MAIT IS in a time dependent manner upon MAIT cell stimulation with THP-1 target cells (Fig. 37). After a timespan of thirty minutes, S100A4 was distributed equally in the cell again. These data suggest a role of S100A4 in IS formation in MAIT cells. Interestingly, MAIT cells express far more S100A4 than NK cells, although the amount of cytolytic granules, granzymes and perforin is significantly lower in MAITs (Tab. 15). Therefore, amounts of S100A4 do not correlate with the number of granules, suggesting an additional role for S100A4 besides possible granule coordination.

In summary, the MAIT cell IS has been shown for the first time, and it displays properties that are similar to the IS of conventional CD8⁺ T cells. Although first light has been shed on the role of S100A4 in synapse formation, and it indeed has been shown to localize to the MAIT:THP-1 interface, its exact role in MAIT cells remains to be elucidated.

In total, proteomic data allows a first glimpse on the novel mechanisms of innate immunity

in MAIT cells, and the generation of a hypothetical step-by-step model on how MAIT activity can be exerted and controlled (Fig. 42). While high abundance of CD98, and the resulting availability of nutrients can already keep MAITs in a state of readiness, their effector molecule profile is dominated by granzymes A, K and M. Upon target cell contact, and recognition of the antigen:MR-1 complex, proteins like secernin-1, Slp2 and S100A4 can promote synapse formation and quick and massive exocytosis of granules. Also, granules converge to the interface between MAIT and target cells, where S100A4 accumulates. After delivery of the cytolytic granules into the target cell, and its subsequent cell death, MAIT activity has to be controlled. MAITs are sensitive to stimulation by cytokines, so especially in a pro-inflammatory environment, overactivity needs to be prevented. Factors like galectin-3 that, upon secretion, induces apoptosis in T cells, or LAAO, which prevents T cell proliferation, can be factors to keep MAIT cells from damaging healthy cells.

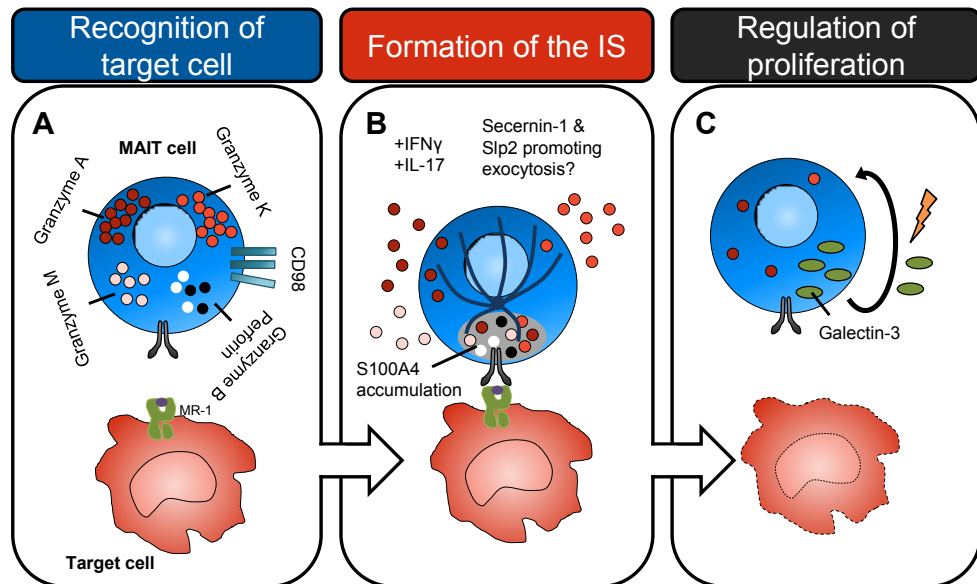


Figure 42 | A first view on MAIT cell IS formation and proliferation control. Although knowledge is still fragmentary, proteomic data from this study allows glimpses on novel mechanisms in MAIT cells, and the generation of a preliminary step-by-step model of MAIT activation. (A) Resting MAIT cells already express high amounts of CD98, that allow high nutrient intake and can keep them in a state allowing quick reaction to stimuli. Also, MAIT cells primarily express granzymes A, K and M. (B) Upon recognition of the target cell, MAIT cells release the granzymes, and additionally cytokines like IFN- γ and IL-17. A pronounced exocytotic response upon stimulation can be supported by the presence of promoting factors like S100A4, secernin-1 and Slp2. Also, the MTOC and the cytolytic granules converge to the target cell. At the interface, S100A4 accumulation can be observed. (C) After the killing of the target cell, MAIT proliferation and activity has to be tightly to controlled to prevent overactivation, especially in a pro-inflammatory environment. Galectin-3 can be a factor that, if secreted, kills active MAIT cells and therefore prevent damage of healthy tissue. This would also explain low numbers of MAIT cells in chronic infections.

5 Summary and outlook

5.1 Coordination of NK effector function by kinases Fyn, CaMKII and PKD

In the first part of the present work, NK cell effector functions were inhibited by chemical perturbation of kinases SFK, CaMKII and PKD2, that had been suggested in a previous study as NK cell signaling components.⁴³ By stimulating primary human NK cells with K562 target cells in PBMC cultures after inhibitor treatment, it could be demonstrated that NK cell degranulation and release of cytokines TNF- α and IFN- γ was indeed reduced (3.1.1, Fig. 13).¹³⁵ Already low amounts of SFK-inhibitor Dasatinib significantly reduced surface expression of CD107a and cytokine secretion. The effect of CaMKII inhibitor CK59 was less pronounced, but also reproducibly decreased effector functions was seen, although the observed effect was more dose-dependent and gradual. Inhibition with CID755673, that is directed against PKD kinases, had the strongest effect on TNF- α -release, but also dose-dependently decreased the number of CD107a⁺ and IFN- γ ⁺ cells. The inhibitor experiments were repeated in cultures of purified NK cells, to reveal effects from other cell types (3.1.2, Fig. 14). In general, results generated in pure NK cells were in accordance with data received in PBMC cultures. For all inhibitors, a dose-dependent decrease of NK cell effector functions was observed. However, it also became apparent that donor variation can have an substantial impact on the results obtained from primary cells, as some donors showed remarkably different reactions on the inhibitor treatment. Taken together, all results further implicate pivotal roles for SFK kinases, CaMKII and PKD kinases in NK cells activation.

However, further investigation of the role of these kinases in NK cell function is of great interest, as the understanding of NK cell signaling is far from complete. Other methods, like RNA interference or CRISPR/Cas-mediated gene editing, might yield useful complementary data on NK cell activity. These methods could be used to specifically silence or delete genes of the investigated kinases, and therefore rule out any side-effects by the highly specific inhibitors. Another possibility to shed further light on the role of the described kinases SFK/Fyn, CaMKII and PKD is the overexpression of mutants. For example, point mutation variants that can not be phosphorylated at the described sites, or mutants that are constitutively active by

mutations that mimic constant phosphorylation. However, the application of methods that directly manipulate genetic material in primary cells, has proven to be difficult. It is of course possible to conduct experiments like this with NK cell lines like NK92, but the situation in immortalized cell lines doesn't always reflect the situation in primary cell material or even *in vivo*.

For a possible clinical application against leukemia or autoimmune-diseases, as discussed in 4.1.3, the effect of the used kinase inhibitors could be investigated in animal models for NK-LGL.²⁵⁷ Also, the NK cell line NKL is derived from NK-LGL²⁵⁸ and its reaction to treatment with inhibitors could also yield primary results for a possible use of the chemicals in therapy.

5.2 Proteomic analysis reveals novel mechanisms of innate immunity in MAIT cells

In the second part, mass spectrometry was used to comparatively analyze the proteome of primary human MAIT, NK and conventional, non-MAIT CD8⁺ (cCD8⁺) T cells and the proteome for primary human MAIT cells was defined for the very first time. Also, proteomic workflows were established to successfully handle low amounts of cells that can be expected when isolating cell subsets from human buffy coats (3.4). In total, over 5500 proteins could be identified from five different healthy human donors, with 2600 being commonly identified in all experiments (3.5.2, Fig. 27). For these 5500 proteins, regulation factors could be calculated. The proteins that were identified in all donors that showed similar distribution, although also donor variation became apparent (3.5.3.1, Fig. 30 and 31), that might be a result of infection (4.2.3). Different numbers were found to be robustly regulated between the analyzed cell subsets (3.5.3.2, Tab. 12). From these data, it is possible to state that surprisingly on the level of proteins, MAIT cells are not as closely related to cCD8⁺ T cells as to NK cells (4.2.3). This suggests a phenotype for MAIT cells that is also dominated by proteins that are important for prototypic innate effectors like NK cells. Also, data confirmed a unique set of effector molecules for MAIT cells, with pronounced abundance of granzymes (Gzm) A and K, as well as GzmM (3.5.4.1, Tab. 15). This suggests that resting MAITs are rather pro-inflammatory than cytotoxic and this set of effector molecules can provide a regulatory mechanism to prevent cytotoxicity against unspecific targets (4.2.5.2). Also, systematic analyses of regulated proteins revealed pronounced abundance of proteins that regulate or promote exocytosis (3.5.4.2), and could indicate that MAIT cells themselves possess pronounced mechanisms of exocytosis, enabling them to react more quickly and fiercely upon activation (4.2.5.3). Another mechanism of regulating MAIT activity is most likely their proneness to apoptosis. Systematic analysis showed high abundance of proteins

that are associated with regulation of proliferation (4.2.5.4). These factors might also play a part in restricting MAIT cell responses, even kill adjacent immune cells or enable them to act quickly upon stimulation (4.2.5.4).

Taken together, these data add vital knowledge to further understand the fascinating cell subset of MAIT cells. They show distinct features from conventional cCD8⁺ T cells and that core mechanisms like exocytosis and proliferation are differently regulated. However, our knowledge about the activation, function and phenotype of MAIT cells is far from complete. However, this thesis has laid important foundations for proteomic analysis of small immune cell numbers, and established reproducible experimental set-ups. Now, on the basis of the established protocols, it would be easy to further refine data acquisition. Recently, and during the course of this thesis, technologies with enhanced sample preparation methods were developed, to further increase the sensitivity of proteomics.¹⁴² This might even allow access to low abundant transcription factors that are vital for the MAIT cell phenotype (ROR γ t, PLZF), interleukins (IL-17, IL-2) or other cytokines (TNF- α , IFN- γ) that could not be identified or quantified in the conservative but robust approach of this study.

The situation is similar regarding the quantification method. For this study, the well-defined and robust quantification method iTRAQ was chosen, to establish a completely new protocol. Also here, a most recently developed technique has been suggested to increase the dynamic range of quantification.²⁵⁹ This could help to further differentiate the already defined regulation factors, or identify regulations that were rejected in this study.

It will also be of great interest to examine the novel players and mechanisms in more detail. Do MAIT cells exocytose faster than conventional cells once they are activated? Does secernin-1 really promote exocytosis? What is the exact function of proteins like galectin-3 that are highly upregulated and can potentially induce death in other T cells? However, as in NK cells, genetic manipulation of primary human MAIT cells is not possible. Also, cell lines exists that express the MAIT cell TCR,¹⁰⁵ and so do mouse models with increased numbers of MAITs.^{76, 113, 260} Both would potentially allow to generate knock-out mutants of these proteins, but if the effect would be comparable to primary human cells is obscure. Nevertheless, experiments to analyze if e. g. MAIT cells really express galectin-3 on the surface upon activation, or if secernin-1 or Spl2 do co-localize with the synapse or granules, can be done in human material by flow cytometry or fluorescence microscopy.

This thesis and former studies have proven that proteomics are a valuable tool to characterize primary human immune cells. It is therefore also a possibility to analyze the difference of MAIT cells to even closer related cell types, like NKT cells, or both CD8⁺CD161⁺ and CD8⁺CD161⁻ cells. Furthermore, it might be worth considering to additionally analyze subsets of MAIT cells themselves, like the DN and CD8⁺ MAITs, or the ones differentiated by different

combination of CD8 chains.⁹⁵

Also, following experiments that will be conducted will deal with the exhaustion and depletion of MAIT cells in chronic infections.^{77, 128, 129} The reason why MAIT cells are depleted in the blood of chronic HIV patients is still under debate, and proteomic comparison of the still present cells and the cells from healthy donors will give insights into the reasons for this depletion (cooperation with J. Sandberg, Karolinska Stockholm and M. Eller, MHRP Bethesda). These data will be complemented by data from chronic HCV patients (coop. H. Wedemeyer, MHH Hannover). This thesis has laid a solid basis to understand the changes that can become apparent when comparing exhausted and resting MAIT cells.

Another field of research that is highly interesting is MAIT behavior in *Clostridium difficile* infection (CDI). *Clostridium difficile* is a new emerging pathogen with increasing relevance, especially in nosocomial infections. Although the pathogen is prevalent in the gut, surprisingly the interactions between MAIT cells and *C. difficile* have not been investigated until now. To investigate this connection, it was planned to investigate the *C. difficile*-specific activation of primary human MAIT cells. Although this activation is possible as *C. difficile* is present in the gut and possesses the ability to produce riboflavin,²⁶¹ it has just been suggested⁷⁰ but never shown. Also, it will be analyzed which MR1-binding metabolites are produced by *Clostridium difficile*. Even if the bacteria surprisingly do not induce activation in MAIT cells, it might be possible that they produce inhibiting ligands. Furthermore, and complementary to the data of exhausted MAIT cells in viral infections, it is planned to characterize the phenotype of MAITs and other innate cells in *C. difficile*-infected patients. With the help of transgenic mice, that only express the MAIT-TCR it will also be possible to investigate the impact of MAIT cells on *C. difficile* infection *in vivo*.

5.3 First-time characterization of the MAIT cell immunological synapse

In this thesis, the first observation of the MAIT immunological synapse (IS) was presented. For this, an assay was developed to visualize the interaction between MAIT cell and target cell. This experimental setup led to direct observation of cytotoxic activity, and the identification of novel components of the MAIT IS. Indeed, granules containing perforin localize to the IS (3.6.1, Fig. 34), while the cell polarizes and the MTOC relocates (Fig. 36). Upon activation, calcium-dependent protein S100A4 partly associates with the microtubule skeleton. Also, time-dependent accumulation of S100A4 could be observed at the MAIT IS (3.6.3, Fig. 37). However, the knowledge about MAIT cell IS formation is still scarce. It might of interest to analyze if the formation is differently regulated or executed, when compared to conventional

T cells - kinetically or mechanistically. The method established in this work to analyze the MAIT IS with fluorescence microscopy will allow the analysis of different factors like secernin-1 or Spl2, and if they are recruited to the synapse. Also, the colocalization status of S100A4 and microtubules could be investigated further, and if S100A4 localizes at microtubules and under which circumstances.

Additionally, it is of interest to investigate why S100A4 is so prominently expressed in MAIT cells. It is also highly expressed in extremely cytotoxic CD56^{dim} NK cells¹⁹ and is suggested to coordinate granule release. So, further colocalization experiments of S100A4 and markers for granules like CD107a might increase our knowledge about the function of this protein. This would also be true for genetically manipulated cells, but as stated in the chapter before, this is not a trivial experiment and might even be hard to accomplish in primary cells.

APPENDIX

5 Summary and outlook

UniProt Accession	Description	Unique Peptides	Unique spectra	MAIT:NK	MAIT/CD8	NK/CD8	donors regulated		
							MAIT:NK	MAIT:cCD8	NK:cCD8
Q14874	[3-methyl-2-oxobutanoate dehydrogenase] kinase, mitochondrial	1	1	NA	NA	NA			
P54922	[Protein ADP-ribosylarginine] hydrolase	1	1	NA	NA	NA			
Q15118	[Pyruvate dehydrogenase (acetyl-transferring)] kinase isozyme 1	3	8	0.18	-0.63	-0.61			
Q15120	[Pyruvate dehydrogenase (acetyl-transferring)] kinase isozyme 3	6	22	0.63	0.56	-0.33	5	5	
Q9P0J1	[Pyruvate dehydrogenase]-phosphatase 1, mitochondrial	7	13	0.05	0.08	0.00			
Q04446	1,4-alpha-glucan-branching enzyme	7	27	0.02	0.03	0.02			
P61604	10 kDa heat shock protein, mitochondrial	13	236	0.27	-0.33	-0.52			
Q15029	116 kDa U5 small nuclear ribonucleoprotein component	31	194	0.01	-0.10	-0.04			
Q9NRX4	14 kDa phosphohistidine phosphatase	2	18	-0.57	-0.18	-0.02			
P31946	14-3-3 protein beta/alpha	9	411	-0.12	-0.17	-0.26			
P62258	14-3-3 protein epsilon	12	251	-0.11	-0.10	-0.03			
Q04917	14-3-3 protein eta	9	261	0.43	0.64	0.17		4	
P61981	14-3-3 protein gamma	7	319	0.38	0.10	-0.18			
P31947	14-3-3 protein sigma	1	180	5.01	3.30	-1.70			
P27348	14-3-3 protein theta	13	369	0.39	0.59	0.19		4	
P63104	14-3-3 protein zeta/delta	17	736	-0.14	0.10	0.06			
O60613	15 kDa selenoprotein	4	9	-0.14	0.16	0.23			
Q9C0C2	182 kDa tankyrase-1-binding protein	1	3	0.30	-0.23	-0.53			
Q99943	1-acyl-sn-glycerol-3-phosphate acyltransferase alpha	2	3	-0.26	-0.35	-0.09			
Q9NUQ2	1-acyl-sn-glycerol-3-phosphate acyltransferase epsilon	4	14	0.45	0.08	-0.28			
Q9NRZ7	1-acyl-sn-glycerol-3-phosphate acyltransferase gamma	1	1	-0.23	-0.20	0.04			
Q9Y2I7	1-phosphatidylinositol 3-phosphate 5-kinase	1	7	NA	NA	NA			
Q00722	1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase beta-2	7	24	-0.30	0.03	0.40			
Q01970	1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase beta-3	1	3	0.26	0.61	0.36			
P51178	1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase delta-1	1	1	0.16	0.13	-0.03			
Q4KWH8	1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase eta-1	1	13	0.12	0.37	0.23			
P19174	1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase gamma-1	11	22	0.84	0.22	-0.55	3		4
P16885	1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase gamma-2	9	32	-2.00	0.13	1.99	4		4
P09543	2',3'-cyclic-nucleotide 3'-phosphodiesterase	6	24	-0.18	0.15	0.32			
Q16698	2,4-dienoyl-CoA reductase, mitochondrial	17	169	0.08	0.15	0.04			
Q6L8Q7	2',5'-phosphodiesterase 12	8	34	0.10	-0.11	-0.29			
Q05823	2-5A-dependent ribonuclease	3	4	-0.12	-0.08	0.29			
P00973	2'-5'-oligoadenylate synthase 1	1	1	-0.18	0.20	0.38			
P29728	2'-5'-oligoadenylate synthase 2	6	20	-0.01	0.14	0.12			
Q9Y6K5	2'-5'-oligoadenylate synthase 3	5	17	0.30	0.16	-0.14			
Q15646	2'-5'-oligoadenylate synthase-like protein	4	8	-0.23	0.32	0.49			
P62333	26S protease regulatory subunit 10B	16	86	0.15	0.03	-0.10			
P62191	26S protease regulatory subunit 4	18	119	0.10	-0.09	-0.15			
P17980	26S protease regulatory subunit 6A	24	144	0.02	-0.11	-0.14			
P43686	26S protease regulatory subunit 6B	11	46	0.18	0.03	-0.08			
P35998	26S protease regulatory subunit 7	22	132	0.08	-0.04	-0.19			
P62195	26S protease regulatory subunit 8	12	100	0.04	-0.02	-0.06			
Q99460	26S proteasome non-ATPase regulatory subunit 1	17	70	0.06	0.06	0.01			
O75832	26S proteasome non-ATPase regulatory subunit 10	8	53	0.25	0.05	-0.16			
O00231	26S proteasome non-ATPase regulatory subunit 11	13	72	0.10	-0.03	-0.18			
O00232	26S proteasome non-ATPase regulatory subunit 12	10	49	0.11	-0.07	-0.24			
Q9UNM6	26S proteasome non-ATPase regulatory subunit 13	7	27	0.12	0.07	-0.09			
O00487	26S proteasome non-ATPase regulatory subunit 14	5	35	0.19	-0.02	-0.19			
Q13200	26S proteasome non-ATPase regulatory subunit 2	19	65	0.22	0.07	-0.14			
O43242	26S proteasome non-ATPase regulatory subunit 3	13	41	0.16	0.18	-0.11			
P55036	26S proteasome non-ATPase regulatory subunit 4	11	75	0.06	-0.04	-0.03			
Q16401	26S proteasome non-ATPase regulatory subunit 5	9	48	0.10	-0.04	-0.16			
Q15008	26S proteasome non-ATPase regulatory subunit 6	8	44	0.12	0.09	-0.03			
P51665	26S proteasome non-ATPase regulatory subunit 7	6	26	0.28	-0.10	-0.13			
P48556	26S proteasome non-ATPase regulatory subunit 8	3	4	0.26	0.05	-0.26			
O00233	26S proteasome non-ATPase regulatory subunit 9	8	53	-0.05	0.00	0.15			
Q13442	28 kDa heat- and acid-stable phosphoprotein	11	68	0.01	0.08	0.08			
P82912	28S ribosomal protein S11, mitochondrial	1	1	0.33	0.20	-0.13			
O15235	28S ribosomal protein S12, mitochondrial	1	1	0.00	0.18	0.18			
O60783	28S ribosomal protein S14, mitochondrial	1	3	-0.04	-0.40	-0.37			
P82914	28S ribosomal protein S15, mitochondrial	2	22	0.63	-0.03	-0.23	3		
Q9Y3D3	28S ribosomal protein S16, mitochondrial	1	3	-0.30	0.16	0.40			
Q9Y2R5	28S ribosomal protein S17, mitochondrial	2	14	0.25	0.12	-0.48			
Q9NVS2	28S ribosomal protein S18a, mitochondrial	3	5	0.18	-0.08	-0.13			
Q9Y676	28S ribosomal protein S18b, mitochondrial	1	1	-0.10	-0.08	0.02			
P82921	28S ribosomal protein S21, mitochondrial	3	9	-0.17	-0.13	0.11			
P82650	28S ribosomal protein S22, mitochondrial	3	11	0.12	-0.08	-0.21			
Q9Y3D9	28S ribosomal protein S23, mitochondrial	5	8	-0.01	0.03	0.04			
P82663	28S ribosomal protein S25, mitochondrial	1	4	0.27	0.07	-0.06			
Q9BYN8	28S ribosomal protein S26, mitochondrial	2	3	NA	NA	NA			
Q92552	28S ribosomal protein S27, mitochondrial	5	6	0.36	0.09	-0.27			
Q9Y2Q9	28S ribosomal protein S28, mitochondrial	2	2	-0.12	-0.11	0.02			
P51398	28S ribosomal protein S29, mitochondrial	3	11	0.03	0.02	0.00			
Q9NP92	28S ribosomal protein S30, mitochondrial	1	1	0.16	-0.22	-0.39			
Q92665	28S ribosomal protein S31, mitochondrial	6	18	0.11	-0.02	-0.07			
Q9Y291	28S ribosomal protein S33, mitochondrial	1	5	-0.23	-0.09	0.08			
P82930	28S ribosomal protein S34, mitochondrial	3	6	0.10	-0.59	-0.70			
P82673	28S ribosomal protein S35, mitochondrial	2	4	0.27	0.16	-0.20			
P82909	28S ribosomal protein S36, mitochondrial	7	37	0.00	-0.03	-0.04			
P82675	28S ribosomal protein S5, mitochondrial	2	10	0.06	-0.18	-0.11			

Q9Y2R9	28S ribosomal protein S7, mitochondrial	3	3	-0.01	0.02	0.02			
P82933	28S ribosomal protein S9, mitochondrial	4	7	-0.02	0.07	0.05			
Q96S25	2-aminoethanethiol dioxygenase	5	12	-0.30	0.02	0.20			
O43598	2'-deoxynucleoside 5'-phosphate N-hydrolase 1	4	13	0.43	-0.52	-0.94			3
Q02218	2-oxoglutarate dehydrogenase, mitochondrial	25	160	0.58	0.35	-0.14	5		
P12694	2-oxoisovalerate dehydrogenase subunit alpha, mitochondrial	7	30	0.25	0.10	-0.19			
O95861	3'(2'),5'-bisphosphate nucleotidase 1	14	51	0.11	-0.01	-0.06			
Q8IV48	3'-5' exoribonuclease 1	1	1	0.13	0.06	-0.07			
Q9BYD6	39S ribosomal protein L1, mitochondrial	5	7	0.39	-0.06	-0.40			
Q9Y3B7	39S ribosomal protein L11, mitochondrial	8	29	0.09	-0.06	-0.19			
P52815	39S ribosomal protein L12, mitochondrial	9	49	0.11	0.00	-0.12			
Q9BYD1	39S ribosomal protein L13, mitochondrial	2	4	-0.21	-0.52	-0.32			
Q6P1L8	39S ribosomal protein L14, mitochondrial	4	10	0.06	-0.01	-0.01			
Q9P015	39S ribosomal protein L15, mitochondrial	1	1	0.33	-0.23	-0.55			
Q9NX20	39S ribosomal protein L16, mitochondrial	3	7	0.06	-0.37	-0.54			
Q9NRX2	39S ribosomal protein L17, mitochondrial	2	5	0.00	-0.38	-0.37			
Q9H0U6	39S ribosomal protein L18, mitochondrial	1	2	0.41	0.06	-0.36			
P49406	39S ribosomal protein L19, mitochondrial	3	5	0.25	0.02	-0.13			
Q5T653	39S ribosomal protein L2, mitochondrial	3	9	-0.20	0.17	0.31			
Q7Z2W9	39S ribosomal protein L21, mitochondrial	1	1	NA	NA	NA			
Q9NWU5	39S ribosomal protein L22, mitochondrial	3	12	0.17	0.13	-0.03			
Q16540	39S ribosomal protein L23, mitochondrial	2	8	0.16	0.12	-0.05			
Q96A35	39S ribosomal protein L24, mitochondrial	1	3	0.24	0.02	-0.26			
Q9P0M9	39S ribosomal protein L27, mitochondrial	3	10	0.27	0.09	-0.18			
P09001	39S ribosomal protein L3, mitochondrial	1	1	0.50	0.22	-0.28			
Q8TCC3	39S ribosomal protein L30, mitochondrial	1	3	0.14	-0.10	-0.24			
O75394	39S ribosomal protein L33, mitochondrial	1	5	-0.72	-0.19	0.54			
Q9BQ48	39S ribosomal protein L34, mitochondrial	1	1	-0.07	-0.36	-0.30			
Q9BZE1	39S ribosomal protein L37, mitochondrial	4	8	0.38	0.03	-0.39			
Q96DV4	39S ribosomal protein L38, mitochondrial	5	8	0.03	-0.22	-0.17			
Q9NYK5	39S ribosomal protein L39, mitochondrial	3	8	0.21	-0.05	-0.21			
Q9BYD3	39S ribosomal protein L4, mitochondrial	3	11	0.08	0.06	-0.07			
Q9NQ50	39S ribosomal protein L40, mitochondrial	3	9	-0.04	-0.21	-0.24			
Q8IXM3	39S ribosomal protein L41, mitochondrial	1	3	0.56	0.11	-0.45			
Q9Y6G3	39S ribosomal protein L42, mitochondrial	2	2	-0.38	0.32	0.71			
Q8N983	39S ribosomal protein L43, mitochondrial	3	9	0.36	0.12	-0.11			
Q9H9J2	39S ribosomal protein L44, mitochondrial	3	9	0.30	0.09	-0.30			
Q9BRJ2	39S ribosomal protein L45, mitochondrial	3	7	-0.35	-0.63	-0.27			
Q9H2W6	39S ribosomal protein L46, mitochondrial	3	10	0.08	-0.04	-0.13			
Q9HD33	39S ribosomal protein L47, mitochondrial	1	4	NA	NA	NA			
Q96GC5	39S ribosomal protein L48, mitochondrial	2	7	0.16	-0.10	-0.32			
Q13405	39S ribosomal protein L49, mitochondrial	4	14	0.45	0.09	-0.31			
Q8N5N7	39S ribosomal protein L50, mitochondrial	2	7	0.37	-0.06	-0.43			
Q96EL3	39S ribosomal protein L53, mitochondrial	2	4	-0.02	-0.18	-0.16			
Q6P161	39S ribosomal protein L54, mitochondrial	1	1	-1.80	-0.90	0.92			
Q7Z7F7	39S ribosomal protein L55, mitochondrial	2	7	0.16	0.02	-0.20			
Q9BYD2	39S ribosomal protein L9, mitochondrial	4	7	0.20	-0.15	-0.12			
Q99714	3-hydroxyacyl-CoA dehydrogenase type-2	15	297	0.12	0.01	-0.11			
Q9BUT1	3-hydroxybutyrate dehydrogenase type 2	5	32	0.16	-0.31	-0.44			
P31937	3-hydroxyisobutyrate dehydrogenase, mitochondrial	8	72	0.27	-0.08	-0.42			
Q6NVY1	3-hydroxyisobutyryl-CoA hydrolase, mitochondrial	6	25	0.10	0.10	0.01			
P42765	3-ketoacyl-CoA thiolase, mitochondrial	28	307	0.25	0.81	0.53	5		4
P09110	3-ketoacyl-CoA thiolase, peroxisomal	6	10	-0.19	-0.12	-0.01			
Q06136	3-ketodihydrosphingosine reductase	1	4	0.97	0.62	-0.34			
P25325	3-mercaptopyruvate sulfurtransferase	6	20	-0.55	0.31	0.71	4		5
Q9NWU1	3-oxoacyl-[acyl-carrier-protein] synthase, mitochondrial	4	16	0.11	0.00	-0.38			
O15530	3-phosphoinositide-dependent protein kinase 1	5	17	-0.04	-0.03	0.17			
P46783	40S ribosomal protein S10	8	130	0.37	0.02	-0.37			
P62280	40S ribosomal protein S11	18	166	0.44	0.05	-0.47			5
P25398	40S ribosomal protein S12	11	86	0.40	-0.02	-0.48			
P62277	40S ribosomal protein S13	13	98	0.45	-0.07	-0.47			5
P62263	40S ribosomal protein S14	8	183	0.18	-0.01	-0.22			
P62841	40S ribosomal protein S15	3	7	0.53	0.00	-0.59			
P62244	40S ribosomal protein S15a	12	95	0.28	0.05	-0.36			
P62249	40S ribosomal protein S16	12	287	0.40	-0.05	-0.58			5
P0CW22	40S ribosomal protein S17-like	9	125	0.27	0.01	-0.27			
P62269	40S ribosomal protein S18	12	199	0.48	0.04	-0.41			
P39019	40S ribosomal protein S19	15	277	0.29	-0.09	-0.58			
P15880	40S ribosomal protein S2	20	207	0.54	-0.09	-0.55			5
P60866	40S ribosomal protein S20	6	55	0.30	-0.04	-0.42			
P63220	40S ribosomal protein S21	8	126	0.16	-0.11	-0.24			
P62266	40S ribosomal protein S23	7	118	0.48	-0.08	-0.50			
P62847	40S ribosomal protein S24	6	80	0.19	-0.12	-0.20			
P62851	40S ribosomal protein S25	9	90	0.29	-0.18	-0.44			
P62854	40S ribosomal protein S26	2	51	0.71	0.07	-0.49	4		
P42677	40S ribosomal protein S27	1	54	0.41	0.13	-0.15			
Q71UM5	40S ribosomal protein S27-like	1	52	0.01	-0.28	-0.28			
P62857	40S ribosomal protein S28	5	161	0.63	0.02	-0.33	3		
P62273	40S ribosomal protein S29	2	3	-0.04	-0.85	-0.82			
P23396	40S ribosomal protein S3	22	261	0.72	0.05	-0.52	3		5
P62861	40S ribosomal protein S30	2	58	0.14	-0.07	-0.20			
P61247	40S ribosomal protein S3a	24	312	0.57	-0.03	-0.57	5		5
P62701	40S ribosomal protein S4, X isoform	14	228	0.41	-0.09	-0.48			
P22090	40S ribosomal protein S4, Y isoform 1	5	34	-0.24	-0.42	-0.19			
P46782	40S ribosomal protein S5	12	77	0.61	-0.14	-0.60			5
P62753	40S ribosomal protein S6	13	114	0.53	0.01	-0.44	4		

P62081	40S ribosomal protein S7	11	129	0.45	-0.05	-0.44			5
P62241	40S ribosomal protein S8	11	141	0.30	0.12	-0.45			
P46781	40S ribosomal protein S9	13	105	0.65	0.12	-0.44	3		
P08865	40S ribosomal protein SA	12	183	0.42	0.10	-0.47			
P80404	4-aminobutyrate aminotransferase, mitochondrial	4	6	0.34	0.71	0.37			
P08195	4F2 cell-surface antigen heavy chain	9	47	1.06	1.14	-0.03	5	5	
P49189	4-trimethylaminobutyraldehyde dehydrogenase	20	167	0.38	-0.10	-0.40			5
Q8TCD5	5'(3')-deoxyribonucleotidase, cytosolic type	1	1	0.65	0.26	-0.38			
O43422	52 kDa repressor of the inhibitor of the protein kinase	1	1	1.29	0.75	-0.53			
Q8IZH2	5'-3' exoribonuclease 1	8	13	-0.14	-0.14	0.15			
Q9H0D6	5'-3' exoribonuclease 2	18	83	-0.01	-0.18	-0.11			
Q00013	55 kDa erythrocyte membrane protein	2	2	-0.03	-0.34	-0.32			
Q13131	5'-AMP-activated protein kinase catalytic subunit alpha-1	4	17	-0.06	0.20	0.29			
P54619	5'-AMP-activated protein kinase subunit gamma-1	4	11	0.05	0.34	0.30			
P49914	5-formyltetrahydrofolate cyclo-ligase	2	5	-0.05	-0.61	-0.37			
Q96CB9	5-methylcytosine rRNA methyltransferase NSUN4	1	1	NA	NA	NA			
P21589	5'-nucleotidase	5	13	0.58	-0.36	-0.88	4		5
Q5TFE4	5'-nucleotidase domain-containing protein 1	6	18	0.41	0.05	-0.43			
Q8IUZ5	5-phosphohydroxy-L-lysine phospho-lyase	4	6	0.20	-0.16	-0.37			
P10809	60 kDa heat shock protein, mitochondrial	45	909	0.27	-0.19	-0.56			5
P10155	60 kDa SS-A/Ro ribonucleoprotein	11	36	-0.02	0.28	0.25			
P05388	60S acidic ribosomal protein P0	15	199	0.58	0.01	-0.58	5		5
P05386	60S acidic ribosomal protein P1	2	55	0.50	-0.18	-0.50			
P05387	60S acidic ribosomal protein P2	6	114	0.49	0.14	-0.15			
Q96D46	60S ribosomal export protein NMD3	1	8	0.21	0.05	-0.34			
P27635	60S ribosomal protein L10	10	152	0.52	0.12	-0.39			
P62906	60S ribosomal protein L10a	11	177	0.52	-0.02	-0.56	5		5
P62913	60S ribosomal protein L11	7	113	0.46	0.07	-0.48			5
P30050	60S ribosomal protein L12	11	167	0.37	-0.02	-0.46			5
P26373	60S ribosomal protein L13	17	185	0.31	0.00	-0.33			
P40429	60S ribosomal protein L13a	12	113	0.44	-0.07	-0.42			5
P50914	60S ribosomal protein L14	11	141	0.45	0.03	-0.54	5		
P61313	60S ribosomal protein L15	6	47	0.70	0.10	-0.66	5		5
P18621	60S ribosomal protein L17	9	136	0.49	-0.07	-0.47			
Q07020	60S ribosomal protein L18	9	100	0.64	0.08	-0.56	5		5
Q02543	60S ribosomal protein L18a	11	106	0.51	0.21	-0.38			
P84098	60S ribosomal protein L19	7	80	0.59	0.11	-0.45	4		
P46778	60S ribosomal protein L21	3	58	0.20	-0.01	-0.12			
P35268	60S ribosomal protein L22	7	77	0.54	0.09	-0.47			4
P62829	60S ribosomal protein L23	10	191	0.26	-0.03	-0.32			
P62750	60S ribosomal protein L23a	11	138	0.60	0.06	-0.45			
P83731	60S ribosomal protein L24	11	169	0.24	-0.16	-0.38			
P61254	60S ribosomal protein L26	7	85	0.24	-0.13	-0.33			
P61353	60S ribosomal protein L27	8	89	0.44	0.07	-0.37			
P46776	60S ribosomal protein L27a	9	130	0.61	0.05	-0.53			
P46779	60S ribosomal protein L28	9	111	0.31	-0.21	-0.43			5
P47914	60S ribosomal protein L29	5	44	0.29	-0.22	-0.57			
P39023	60S ribosomal protein L3	31	226	0.44	0.20	-0.48	5		
P62888	60S ribosomal protein L30	10	155	0.48	-0.03	-0.52			
P62899	60S ribosomal protein L31	6	59	0.35	-0.01	-0.41			
P62910	60S ribosomal protein L32	6	90	0.35	0.02	-0.36			
P49207	60S ribosomal protein L34	9	124	0.48	0.04	-0.56			5
P42766	60S ribosomal protein L35	5	53	0.17	-0.07	-0.45			
P18077	60S ribosomal protein L35a	5	18	0.36	0.22	-0.51			
Q9Y3U8	60S ribosomal protein L36	6	81	0.58	-0.03	-0.46			
P83881	60S ribosomal protein L36a	2	18	0.36	-0.74	-0.97		3	3
Q969Q0	60S ribosomal protein L36a-like	2	15	0.91	0.49	-0.42			
P61927	60S ribosomal protein L37	2	4	0.18	-0.19	-0.40			
P61513	60S ribosomal protein L37a	6	43	0.38	0.06	-0.21			
P63173	60S ribosomal protein L38	5	146	0.15	-0.02	-0.21			
P36578	60S ribosomal protein L4	26	356	0.51	0.01	-0.49	5		5
P46777	60S ribosomal protein L5	21	181	0.42	-0.07	-0.52			5
Q02878	60S ribosomal protein L6	16	163	0.64	-0.07	-0.52	4		5
P18124	60S ribosomal protein L7	15	99	0.58	0.17	-0.46	5		5
P62424	60S ribosomal protein L7a	17	284	0.47	-0.05	-0.43	5		5
Q6DKI1	60S ribosomal protein L7-like 1	5	16	0.34	-0.04	-0.27			
P62917	60S ribosomal protein L8	10	140	0.30	-0.12	-0.44			
P32969	60S ribosomal protein L9	9	69	0.47	-0.01	-0.26			
Q9Y221	60S ribosome subunit biogenesis protein NIP7 homolog	3	3	-0.11	-0.32	-0.22			
Q16875	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 3	5	12	0.23	0.92	0.40		3	
Q01813	6-phosphofructokinase type C	17	70	0.14	-0.03	-0.13			
P17858	6-phosphofructokinase, liver type	13	67	-0.01	-0.01	-0.08			
P08237	6-phosphofructokinase, muscle type	2	6	0.12	-0.41	-0.52			
P52209	6-phosphogluconate dehydrogenase, decarboxylating	13	103	0.04	-0.23	-0.21			
Q95336	6-phosphogluconolactonase	12	161	-0.37	-0.06	0.30			
P36639	7,8-dihydro-8-oxoguanine triphosphatase	1	2	-0.28	-0.19	0.08			
P11021	78 kDa glucose-regulated protein	43	755	-0.10	0.34	0.36			
Q7L2J0	7SK snRNA methylphosphate capping enzyme	6	27	-0.31	-0.45	-0.07			
Q6ZVK8	8-oxo-dGDP phosphatase NUDT18	1	4	NA	NA	NA			
Q9P2A4	ABI gene family member 3	8	37	-0.42	0.35	0.80		5	5
Q8IZP0	Abi interactor 1	4	19	0.47	0.30	-0.17	5		
Q9Y4K1	Absent in melanoma 1 protein	14	24	0.63	0.12	-0.40	4		
A1L0T0	Acetolactate synthase-like protein	4	5	-0.10	-0.20	-0.02			
Q9BWD1	Acetyl-CoA acetyltransferase, cytosolic	11	16	-0.06	-0.27	-0.37			
P24752	Acetyl-CoA acetyltransferase, mitochondrial	21	114	0.78	0.12	-0.47	4		
Q13085	Acetyl-CoA carboxylase 1	1	1	-0.35	0.21	0.57			

Q9NUB1	Acetyl-coenzyme A synthetase 2-like, mitochondrial	7	18	-0.16	0.24	0.26			
Q13510	Acid ceramidase	6	31	-0.46	0.41	0.83			4
Q32M88	Acid trehalase-like protein 1	6	24	-0.24	-0.07	0.28			
Q43427	Acidic fibroblast growth factor intracellular-binding protein	1	1	0.03	0.17	0.12			
P39687	Acidic leucine-rich nuclear phosphoprotein 32 family member A	8	147	-0.02	-0.25	-0.16			
Q92688	Acidic leucine-rich nuclear phosphoprotein 32 family member B	6	74	0.24	-0.29	-0.61			4
Q98TT0	Acidic leucine-rich nuclear phosphoprotein 32 family member E	9	84	0.39	0.17	-0.14			
Q99798	Aconitate hydratase, mitochondrial	29	263	0.13	-0.02	-0.13			
P68032	Actin, alpha cardiac muscle 1	2	2409	-0.23	-0.04	0.18			
P68133	Actin, alpha skeletal muscle	1	2405	NA	NA	NA			
P60709	Actin, cytoplasmic 1	13	4816	-0.10	0.04	0.14			
O14639	Actin-binding LIM protein 1	10	37	0.24	-0.99	-1.08		5	4
O96019	Actin-like protein 6A	11	47	0.12	-0.04	-0.05			
Q9NZ32	Actin-related protein 10	4	15	0.11	-0.07	-0.12			
P61160	Actin-related protein 2	18	221	-0.19	0.11	0.34			
Q92747	Actin-related protein 2/3 complex subunit 1A	4	6	-0.37	0.03	0.40			
O15143	Actin-related protein 2/3 complex subunit 1B	17	246	-0.08	0.03	0.21			
O15144	Actin-related protein 2/3 complex subunit 2	17	164	0.08	0.14	0.32			
O15145	Actin-related protein 2/3 complex subunit 3	9	106	-0.18	0.02	0.04			
P59998	Actin-related protein 2/3 complex subunit 4	9	101	-0.24	0.14	0.39			
O15511	Actin-related protein 2/3 complex subunit 5	11	201	-0.40	-0.23	0.13			
Q9BPX5	Actin-related protein 2/3 complex subunit 5-like protein	5	63	-0.70	0.66	1.47	5	5	5
P61158	Actin-related protein 3	20	400	-0.26	0.12	0.34			
Q9P1U1	Actin-related protein 3B	1	52	-0.51	-0.47	0.03			
Q9H9F9	Actin-related protein 5	3	9	0.04	-0.09	0.02			
Q9GZN1	Actin-related protein 6	1	1	-0.32	-0.04	0.29			
Q9H981	Actin-related protein 8	3	3	-0.03	0.03	-0.01			
Q07912	Activated CDC42 kinase 1	1	1	-0.43	0.30	0.74			
P53999	Activated RNA polymerase II transcriptional coactivator p15	10	102	-0.08	-0.22	-0.26			
Q15650	Activating signal cointegrator 1	1	2	0.23	0.34	0.10			
Q8N9N2	Activating signal cointegrator 1 complex subunit 1	1	1	-0.15	0.02	0.17			
Q9H1I8	Activating signal cointegrator 1 complex subunit 2	1	1	-1.11	-0.19	0.93			
Q8N3C0	Activating signal cointegrator 1 complex subunit 3	5	5	0.04	0.34	0.28			
Q6VMQ6	Activating transcription factor 7-interacting protein 1	2	9	-0.29	-0.02	0.39			
O95433	Activator of 90 kDa heat shock protein ATPase homolog 1	11	34	0.23	-0.07	-0.17			
Q9ULW3	Activator of basal transcription 1	5	8	0.25	-0.08	-0.37			
Q12979	Active breakpoint cluster region-related protein	2	8	0.12	0.20	0.08			
Q86WX3	Active regulator of SIRT1	3	10	-0.10	-0.10	-0.07			
Q9H2P0	Activity-dependent neuroprotector homeobox protein	12	32	-0.19	-0.27	-0.12			
O14561	Acyl carrier protein, mitochondrial	2	35	0.25	0.10	-0.22			
P13798	Acylamino-acid-releasing enzyme	13	94	-0.07	-0.03	-0.03			
Q6JQN1	Acyl-CoA dehydrogenase family member 10	1	2	0.40	-0.21	-0.60			
Q9H845	Acyl-CoA dehydrogenase family member 9, mitochondrial	2	7	0.46	0.34	-0.11			
Q96CM8	Acyl-CoA synthetase family member 2, mitochondrial	3	8	-0.06	-0.12	0.08			
Q4G176	Acyl-CoA synthetase family member 3, mitochondrial	9	14	0.33	0.18	-0.37			
Q92604	Acyl-CoA:lysophosphatidylglycerol acyltransferase 1	1	1	-1.03	0.58	1.61			
Q9BR61	Acyl-CoA-binding domain-containing protein 6	1	1	0.04	0.05	0.02			
P07108	Acyl-CoA-binding protein	4	28	-0.12	0.24	0.65			3
Q86TX2	Acyl-coenzyme A thioesterase 1	8	42	-0.13	-0.12	0.01			
Q9NPJ3	Acyl-coenzyme A thioesterase 13	5	45	0.29	-0.01	-0.25			
O14734	Acyl-coenzyme A thioesterase 8	1	1	-0.55	-0.36	0.19			
Q9Y305	Acyl-coenzyme A thioesterase 9, mitochondrial	4	16	0.35	0.66	0.26		3	
Q5T1C6	Acyl-coenzyme A thioesterase THEM4	2	6	0.42	0.12	-0.46			
Q53H12	Acylglycerol kinase, mitochondrial	8	29	-0.40	0.32	0.58			4
P28039	Acylglycerol kinase, mitochondrial	1	1	-0.52	0.21	0.73			
P07311	Acylphosphatase-1	1	5	0.06	-0.09	0.01			
P14621	Acylphosphatase-2	2	10	-0.26	-0.04	0.18			
O75608	Acyl-protein thioesterase 1	5	28	-0.04	0.34	0.47			
O95372	Acyl-protein thioesterase 2	8	41	0.23	-0.08	-0.28			
Q6P587	Acylpyruvase FAHD1, mitochondrial	5	17	-0.25	0.01	-0.02			
P82987	ADAMTS-like protein 3	1	1	2.05	2.80	0.76			
Q6UY14	ADAMTS-like protein 4	1	1	-0.08	-0.02	0.07			
P46108	Adapter molecule crk	1	1	-1.10	-0.38	0.73			
Q8NC96	Adaptin ear-binding coat-associated protein 1	1	5	0.12	-0.07	-0.18			
Q9NVZ3	Adaptin ear-binding coat-associated protein 2	9	41	-0.16	-0.05	0.01			
P07741	Adenine phosphoribosyltransferase	7	85	0.68	-0.05	-0.73	4		5
P00813	Adenosine deaminase	18	74	-0.29	0.31	0.64			4
Q9NZK5	Adenosine deaminase CECR1	7	17	0.18	0.33	0.23			
P55263	Adenosine kinase	6	25	0.54	-0.19	-0.73			5
P23526	Adenosylhomocysteinase	16	96	0.21	-0.69	-0.79		3	5
P51828	Adenylyl cyclase type 7	1	1	-0.33	0.19	0.51			
P54819	Adenylyl cyclase 2, mitochondrial	16	232	-0.07	-0.11	0.01			
Q9Y6K8	Adenylyl cyclase isoenzyme 5	2	5	-0.42	-1.13	-0.72			
P30566	Adenylosuccinate lyase	10	36	0.27	-0.27	-0.43			5
P30520	Adenylosuccinate synthetase isozyme 2	15	71	-0.19	0.03	0.29			
Q01518	Adenylyl cyclase-associated protein 1	33	454	-0.07	0.01	0.10			
O95396	Adenylyltransferase and sulfurtransferase MOCS3	4	6	-0.14	-0.19	-0.05			
Q9HDC9	Adipocyte plasma membrane-associated protein	12	89	-0.69	0.75	1.28	3	5	4
P12235	ADP/ATP translocase 1	2	51	0.19	0.12	0.12			
P05141	ADP/ATP translocase 2	3	104	-0.20	0.00	0.12			
P12236	ADP/ATP translocase 3	2	89	0.38	0.16	-0.14			
Q9BRR6	ADP-dependent glucokinase	3	18	-0.18	0.28	0.06			
Q9BW91	ADP-ribose pyrophosphatase, mitochondrial	1	1	0.12	-0.17	-0.28			
P28907	ADP-ribosyl cyclase 1	3	5	-1.93	-0.22	1.70			
P61204	ADP-ribosylation factor 3	4	35	0.04	0.28	0.31			
P18085	ADP-ribosylation factor 4	1	19	0.14	0.36	-0.04			

P84085	ADP-ribosylation factor 5	1	33	-0.07	0.11	0.02			
P62330	ADP-ribosylation factor 6	5	25	0.03	1.02	0.56		3	
Q8N6T3	ADP-ribosylation factor GTPase-activating protein 1	6	16	0.06	0.23	0.18			
Q8N6H7	ADP-ribosylation factor GTPase-activating protein 2	13	67	-0.16	0.00	0.18			
Q9NP61	ADP-ribosylation factor GTPase-activating protein 3	6	18	-0.09	0.65	0.57		5	5
Q9UJY5	ADP-ribosylation factor-binding protein GGA1	3	8	-0.14	-0.01	0.30			
Q9UJY4	ADP-ribosylation factor-binding protein GGA2	4	14	0.04	0.29	0.08			
Q9NZ52	ADP-ribosylation factor-binding protein GGA3	3	11	0.10	0.19	0.10			
Q9NXU5	ADP-ribosylation factor-like protein 15	1	3	-0.07	0.27	0.41			
P36404	ADP-ribosylation factor-like protein 2	2	9	0.34	-0.33	-0.63			
Q9Y2Y0	ADP-ribosylation factor-like protein 2-binding protein	1	1	1.43	0.68	-0.73			
P36405	ADP-ribosylation factor-like protein 3	3	21	0.77	0.70	-0.30	5		5
Q66PJ3	ADP-ribosylation factor-like protein 6-interacting protein 4	6	20	-0.04	-0.48	-0.45			
Q96BM9	ADP-ribosylation factor-like protein 8A	1	3	-0.76	0.25	1.01			
Q9NVJ2	ADP-ribosylation factor-like protein 8B	3	19	-0.23	0.22	0.51			
Q13795	ADP-ribosylation factor-related protein 1	2	2	-0.39	-0.02	0.36			
Q9UKK9	ADP-sugar pyrophosphatase	7	78	0.09	-0.09	-0.23			
Q96AP0	Adrenocortical dysplasia protein homolog	2	7	-0.10	0.03	0.18			
P10109	Adrenodoxin, mitochondrial	1	8	0.91	0.12	-0.78			
Q9UHB7	AF4/FMR2 family member 4	2	4	0.03	-0.08	-0.07			
P43652	Afamin	1	5	1.16	1.28	0.13			
Q9Y4W6	AFG3-like protein 2	20	75	0.16	-0.06	-0.27			
O43488	Aflatoxin B1 aldehyde reductase member 2	8	97	0.00	0.06	0.03			
Q6ULP2	Aftiphilin	4	6	-0.03	0.00	0.04			
O00170	AH receptor-interacting protein	14	91	0.13	0.03	-0.21			
O43572	A-kinase anchor protein 10, mitochondrial	1	3	-0.25	-0.03	-0.04			
Q9UKA4	A-kinase anchor protein 11	1	1	-0.37	-0.09	0.26			
Q12802	A-kinase anchor protein 13	33	103	-0.09	0.01	0.10			
Q02040	A-kinase anchor protein 17A	2	3	0.11	0.18	0.07			
Q9P0M2	A-kinase anchor protein 7 isoform gamma	1	2	-0.19	-0.27	-0.09			
O43823	A-kinase anchor protein 8	6	18	-0.28	-0.06	0.17			
Q9ULX6	A-kinase anchor protein 8-like	8	36	-0.17	-0.08	0.05			
Q99996	A-kinase anchor protein 9	14	36	0.14	0.05	-0.09			
Q9NRG9	Aladin	5	6	-0.24	0.14	0.16			
P49588	Alanine--tRNA ligase, cytoplasmic	29	98	0.09	-0.18	-0.17			
Q5JTZ9	Alanine--tRNA ligase, mitochondrial	10	24	0.12	-0.09	-0.04			
Q9BTE6	Alanyl-tRNA editing protein Aarsd1	4	12	-0.10	-0.31	-0.22			
P14550	Alcohol dehydrogenase	13	114	0.36	0.07	-0.27			
P11766	Alcohol dehydrogenase class-3	13	77	0.21	-0.18	-0.24			
Q8IZ83	Aldehyde dehydrogenase family 16 member A1	11	57	-0.12	-0.15	-0.02			
P30837	Aldehyde dehydrogenase X, mitochondrial	6	7	0.48	0.15	-0.35			
P42330	Aldo-keto reductase family 1 member C3	11	92	-1.62	-0.04	1.51	5		5
Q96C23	Aldose 1-epimerase	7	27	1.40	0.90	-0.40	5		5
P15121	Aldose reductase	14	147	0.07	-0.20	-0.56			
Q96BT7	Alkylated DNA repair protein alkB homolog 8	1	1	0.40	0.31	-0.11			
O00116	Alkylidihydroxyacetonephosphate synthase, peroxisomal	2	4	0.06	0.24	-0.01			
P55008	Allograft inflammatory factor 1	1	1	-0.61	-0.36	0.27			
Q8NFV4	Alpha/beta hydrolase domain-containing protein 11	3	7	0.11	-0.10	-0.20			
Q96IU4	Alpha/beta hydrolase domain-containing protein 14B	8	148	0.52	0.15	-0.43	4		
Q96GS6	Alpha/beta hydrolase domain-containing protein 17A	1	1	-0.50	0.44	0.93			
Q9H553	Alpha-1,3/1,6-mannosyltransferase ALG2	1	2	0.47	0.41	-0.06			
P26572	Alpha-1,3-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase	2	3	0.01	0.21	0.19			
P01011	Alpha-1-antichymotrypsin	7	10	-1.40	0.04	1.47			
P01009	Alpha-1-antitrypsin	6	19	-0.55	0.36	1.04			5
P02765	Alpha-2-HS-glycoprotein	2	106	0.89	0.14	-0.04	3		
P01023	Alpha-2-macroglobulin	3	7	1.03	1.21	0.12			
P30533	Alpha-2-macroglobulin receptor-associated protein	2	2	-0.69	-0.17	0.52			
P12814	Alpha-actinin-1	24	438	0.05	-1.32	-1.54		5	5
O43707	Alpha-actinin-4	41	645	-0.27	1.03	1.29		5	4
P35611	Alpha-adducin	19	102	-0.10	-0.29	-0.21			
Q9UDR5	Alpha-aminoadipic semialdehyde synthase, mitochondrial	1	1	0.05	-0.30	-0.35			
P61163	Alpha-centractin	5	63	0.08	-0.07	-0.13			
O43768	Alpha-endosulfine	5	48	-0.28	-0.69	-0.25			
P06733	Alpha-enolase	39	1256	0.23	-0.18	-0.41			
P02771	Alpha-fetoprotein	3	6	1.01	1.53	-0.09			
Q9NZD4	Alpha-hemoglobin-stabilizing protein	2	2	-0.76	-0.29	0.49			
Q9C0B1	Alpha-ketoglutarate-dependent dioxygenase FTO	2	3	0.70	0.00	-0.69			
P35475	Alpha-L-iduronidase	7	48	-0.57	0.23	0.78			5
Q9NTJ4	Alpha-mannosidase 2C1	2	2	0.13	0.14	0.02			
P17050	Alpha-N-acetylgalactosaminidase	3	5	-0.45	-0.06	0.39			
P54802	Alpha-N-acetylglucosaminidase	4	8	-0.59	0.28	0.94			4
P54920	Alpha-soluble NSF attachment protein	14	57	0.11	0.08	0.07			
P37840	Alpha-synuclein	10	34	-0.63	-0.29	0.26	4		
P40222	Alpha-taxilin	5	13	-0.11	0.21	0.29			
Q8TCU4	Alstrom syndrome protein 1	1	1	0.41	0.60	0.20			
Q06203	Amidophosphoribosyltransferase	7	18	0.09	-0.40	-0.49			
Q12904	Aminoacyl tRNA synthase complex-interacting multifunctional protein 1	10	49	0.11	0.09	-0.10			
Q13155	Aminoacyl tRNA synthase complex-interacting multifunctional protein 2	6	34	0.19	0.08	-0.12			
Q03154	Aminoacylase-1	2	2	-0.33	0.04	0.37			
Q9H4A4	Aminopeptidase B	14	54	-0.05	0.10	0.10			
P15144	Aminopeptidase N	2	3	0.79	0.71	-0.08			
Q08117	Amino-terminal enhancer of split	2	2	-0.17	0.02	0.18			
Q01433	AMP deaminase 2	10	31	0.22	-0.11	-0.26			
Q01432	AMP deaminase 3	3	9	0.92	0.27	-0.65	5		5
Q96FJ0	AMSH-like protease	1	1	0.09	0.24	0.15			
Q99767	Amyloid beta A4 precursor protein-binding family A member 2	1	5	-2.15	-2.67	-0.52			

Q00213	Amyloid beta A4 precursor protein-binding family B member 1	1	4	0.01	-0.80	-0.82			
Q7Z5R6	Amyloid beta A4 precursor protein-binding family B member 1-interacting p	14	76	-0.12	-0.18	-0.15			
Q8TCF1	AN1-type zinc finger protein 1	1	2	-0.01	0.04	0.04			
Q8WV99	AN1-type zinc finger protein 2B	1	2	0.09	0.05	-0.04			
Q6FIF0	AN1-type zinc finger protein 6	2	5	-0.66	-0.06	0.61			3
Q6FJ81	Anamorsin	7	23	-0.15	-0.19	-0.11			
Q9H1A4	Anaphase-promoting complex subunit 1	2	2	0.42	-0.23	-0.65			
Q96DE5	Anaphase-promoting complex subunit 16	1	7	-0.11	0.03	0.10			
Q9UJX4	Anaphase-promoting complex subunit 5	1	1	NA	NA	NA			
Q9UJX3	Anaphase-promoting complex subunit 7	3	8	-0.12	-0.08	0.27			
Q8NHZ8	Anaphase-promoting complex subunit CDC26	1	1	-0.07	-0.37	-0.32			
Q9Y679	Ancient ubiquitous protein 1	3	3	-0.43	-0.80	-0.36			
Q8N7X0	Androglobin	1	1	-1.81	-0.78	1.04			
P04920	Anion exchange protein 2	5	10	0.33	0.29	-0.31			
A6QLG3	Ankyrin repeat and BTB/POZ domain-containing protein BTBD11	5	8	0.56	0.22	-0.34			
Q9P2R3	Ankyrin repeat and FYVE domain-containing protein 1	10	29	0.03	0.19	0.15			
Q8IWZ3	Ankyrin repeat and KH domain-containing protein 1	8	28	-0.09	-0.02	0.14			
Q86XL3	Ankyrin repeat and LEM domain-containing protein 2	2	4	-0.27	0.26	0.53			
Q9NXR5	Ankyrin repeat domain-containing protein 10	1	1	0.39	0.48	0.09			
Q6UB99	Ankyrin repeat domain-containing protein 11	1	1	-0.91	-1.23	-0.32			
Q8IZ07	Ankyrin repeat domain-containing protein 13A	3	5	0.13	0.05	-0.07			
Q6ZTN6	Ankyrin repeat domain-containing protein 13D	2	3	-0.14	-0.05	0.09			
Q75179	Ankyrin repeat domain-containing protein 17	2	12	-0.20	-0.16	0.05			
Q96NW4	Ankyrin repeat domain-containing protein 27	2	4	-0.27	0.22	0.58			
P16157	Ankyrin-1	2	2	-0.87	-0.87	0.01			
Q12955	Ankyrin-3	2	2	0.52	-0.16	-0.68			
P04083	Annexin A1	30	780	0.63	1.22	0.61	5	5	3
P50995	Annexin A11	22	222	0.04	-0.27	-0.33			
P07355	Annexin A2	31	508	0.75	1.32	0.59	5	5	
P12429	Annexin A3	1	3	0.04	-0.77	-0.80			
P09525	Annexin A4	14	108	-0.31	0.81	1.25		5	5
P08758	Annexin A5	19	139	1.92	0.85	-0.93	5	5	5
P08133	Annexin A6	64	1162	-0.28	-0.16	0.13			
P20073	Annexin A7	14	124	0.35	-0.10	-0.49			5
Q9NW15	Anoctamin-10	1	2	-0.13	0.21	0.34			
Q4KMQ2	Anoctamin-6	1	3	NA	NA	NA			
Q03518	Antigen peptide transporter 1	9	116	-0.20	0.16	0.28			
Q03519	Antigen peptide transporter 2	7	54	0.06	0.23	0.17			
Q10567	AP-1 complex subunit beta-1	8	96	-0.06	0.22	0.19			
O43747	AP-1 complex subunit gamma-1	7	17	-0.07	0.30	0.21			
O75843	AP-1 complex subunit gamma-like 2	4	12	-0.13	0.26	0.41			
Q9BX55	AP-1 complex subunit mu-1	5	24	-0.09	0.14	0.17			
P61966	AP-1 complex subunit sigma-1A	2	15	0.17	-0.14	-0.15			
P56377	AP-1 complex subunit sigma-2	3	20	-0.30	0.21	0.56			
O95782	AP-2 complex subunit alpha-1	16	98	-0.36	0.11	0.40			
O94973	AP-2 complex subunit alpha-2	7	50	0.15	0.08	-0.11			
P63010	AP-2 complex subunit beta	12	111	-0.19	0.12	0.21			
Q96CW1	AP-2 complex subunit mu	11	29	0.02	0.26	0.21			
P53680	AP-2 complex subunit sigma	1	4	-0.14	0.05	0.17			
Q2M2I8	AP2-associated protein kinase 1	16	74	0.19	0.07	-0.21			
O00203	AP-3 complex subunit beta-1	15	36	0.22	0.20	-0.03			
O14617	AP-3 complex subunit delta-1	4	6	0.11	0.16	-0.04			
Q9Y2T2	AP-3 complex subunit mu-1	6	17	-0.14	0.19	0.22			
Q92572	AP-3 complex subunit sigma-1	3	14	0.28	0.48	0.20		4	
P59780	AP-3 complex subunit sigma-2	1	1	NA	NA	NA			
Q2VPB7	AP-5 complex subunit beta-1	1	1	-0.29	0.03	0.33			
O43299	AP-5 complex subunit zeta-1	2	5	-0.08	-0.06	0.02			
Q0VD83	Apolipoprotein B receptor	29	162	-0.73	0.65	1.42	5	3	5
P04114	Apolipoprotein B-100	1	4	0.02	-0.12	-0.11			
P02655	Apolipoprotein C-II	1	3	1.50	1.60	0.10			
P02656	Apolipoprotein C-III	2	54	0.21	0.17	-0.04			
P02649	Apolipoprotein E	3	5	1.41	1.72	0.33			
Q9BQE5	Apolipoprotein L2	6	42	-0.30	0.78	1.12		4	4
O95236	Apolipoprotein L3	5	5	0.79	0.51	-0.27			
Q9BUR5	Apolipoprotein O	2	6	0.28	0.15	-0.08			
Q6UXV4	Apolipoprotein O-like	5	9	0.02	-0.24	-0.34			
Q9BZZ5	Apoptosis inhibitor 5	13	70	-0.01	-0.15	-0.16			
Q07812	Apoptosis regulator BAX	8	95	-0.21	-0.02	0.03			
P10415	Apoptosis regulator Bcl-2	2	8	0.31	-0.35	-0.74			3
Q9ULZ3	Apoptosis-associated speck-like protein containing a CARD	5	24	-0.46	0.43	0.37			
O95831	Apoptosis-inducing factor 1, mitochondrial	21	135	0.11	0.01	-0.16			
Q9UKV3	Apoptotic chromatin condensation inducer in the nucleus	33	202	-0.25	-0.25	0.02			
O14727	Apoptotic protease-activating factor 1	2	2	0.04	0.15	0.10			
Q7Z2E3	Aprataxin	3	4	-0.21	-0.12	0.10			
P20292	Arachidonate 5-lipoxygenase-activating protein	1	14	NA	NA	NA			
Q9Y2X7	ARF GTPase-activating protein GIT1	6	21	0.09	0.01	-0.09			
Q14161	ARF GTPase-activating protein GIT2	8	31	0.02	0.14	0.20			
P53367	Arfapin-1	6	11	-0.51	0.24	0.69	4		5
P52594	Arf-GAP domain and FG repeat-containing protein 1	6	29	0.09	0.00	-0.06			
O95081	Arf-GAP domain and FG repeat-containing protein 2	4	9	0.07	0.17	0.24			
Q15027	Arf-GAP with coiled-coil, ANK repeat and PH domain-containing protein 1	20	84	0.22	-0.04	-0.14			
Q15057	Arf-GAP with coiled-coil, ANK repeat and PH domain-containing protein 2	16	29	0.02	0.14	0.22			
O75689	Arf-GAP with dual PH domain-containing protein 1	3	6	-0.55	0.42	0.97			
Q99490	Arf-GAP with GTPase, ANK repeat and PH domain-containing protein 2	7	24	0.24	0.29	0.05			
Q96P47	Arf-GAP with GTPase, ANK repeat and PH domain-containing protein 3	1	3	-0.55	-0.12	0.57			
Q96P48	Arf-GAP with Rho-GAP domain, ANK repeat and PH domain-containing prot	8	19	-0.59	0.14	0.64	4		3

Q8WWN8	Arf-GAP with Rho-GAP domain, ANK repeat and PH domain-containing prot	1	1	-0.32	-0.13	0.17			
Q9ULH1	Arf-GAP with SH3 domain, ANK repeat and PH domain-containing protein 1	4	11	-0.22	-0.42	0.19			
P05089	Arginase-1	4	7	0.99	0.79	-0.36			
Q9NWB6	Arginine and glutamate-rich protein 1	6	28	-0.20	-0.29	0.05			
Q7L412	Arginine/serine-rich coiled-coil protein 2	6	58	-0.18	-0.08	0.12			
Q8TF01	Arginine/serine-rich protein PNISR	3	8	-0.06	-0.59	-0.65		3	3
Q9P2R6	Arginine-glutamic acid dipeptide repeats protein	2	2	0.11	-0.33	-0.45			
P54136	Arginine--tRNA ligase, cytoplasmic	17	81	0.42	0.09	-0.29			
P04424	Argininosuccinate lyase	5	16	-0.52	0.30	0.84			4
O95260	Arginyl-tRNA--protein transferase 1	5	6	0.11	-0.18	-0.24			
Q9NVT9	Armadillo repeat-containing protein 1	1	1	-0.65	-0.06	0.58			
Q8N2F6	Armadillo repeat-containing protein 10	2	5	0.42	0.22	-0.17			
Q6NXE6	Armadillo repeat-containing protein 6	2	2	-0.41	0.16	0.54			
Q8IUR7	Armadillo repeat-containing protein 8	2	3	0.20	0.33	0.13			
Q7L311	Armadillo repeat-containing X-linked protein 2	1	1	-0.16	-0.36	-0.20			
Q9UH62	Armadillo repeat-containing X-linked protein 3	3	6	0.02	0.61	0.62			
Q8N5T2	Arrestin domain-containing protein 1	2	2	-0.26	0.02	0.27			
P15289	Arylsulfatase A	5	37	-0.15	0.06	0.28			
P15848	Arylsulfatase B	2	2	0.10	0.57	0.47			
Q9BVC5	Ashwin	4	7	-0.14	-0.05	-0.06			
P08243	Asparagine synthetase	1	1	0.05	-0.05	-0.09			
O43776	Asparagine--tRNA ligase, cytoplasmic	8	34	0.24	-0.02	-0.09			
P17174	Aspartate aminotransferase, cytoplasmic	11	78	0.08	-0.02	-0.09			
P00505	Aspartate aminotransferase, mitochondrial	18	134	0.46	-0.05	-0.37			
P14868	Aspartate--tRNA ligase, cytoplasmic	22	89	0.39	0.12	-0.33			
Q6PI48	Aspartate--tRNA ligase, mitochondrial	7	30	0.25	0.16	-0.18			
Q9ULA0	Aspartyl aminopeptidase	11	59	0.38	-0.28	-0.66			5
Q12797	Aspartyl/asparaginyl beta-hydroxylase	1	9	-1.96	-2.79	-0.82			
Q15121	Astrocytic phosphoprotein PEA-15	4	17	-0.34	0.10	0.31			
P54253	Ataxin-1	2	2	-0.78	0.13	0.92			
Q9UBB4	Ataxin-10	4	20	0.02	0.22	0.10			
P0C7T5	Ataxin-1-like	4	6	-0.21	-0.16	0.27			
Q8WWM7	Ataxin-2-like protein	17	49	-0.21	0.07	0.21			
P54252	Ataxin-3	7	33	-0.05	-0.13	-0.12			
O15265	Ataxin-7	2	3	0.05	-0.19	-0.23			
Q6SPF0	Atherin	9	31	-0.28	-0.39	0.08			
Q5TGY3	AT-hook DNA-binding motif-containing protein 1	1	1	-0.56	-0.09	0.48			
Q7Z591	AT-hook-containing transcription factor	19	57	0.05	0.36	0.37			
Q8NH9	Atlastin-2	2	3	0.08	0.65	0.55			
Q6DD88	Atlastin-3	5	17	0.19	0.41	0.26			
O43313	ATM interactor	1	11	-0.46	0.18	0.60			3
P24539	ATP synthase F(0) complex subunit B1, mitochondrial	8	37	0.18	0.13	0.01			
P00846	ATP synthase subunit a	1	2	0.07	-0.11	-0.18			
P25705	ATP synthase subunit alpha, mitochondrial	42	875	0.01	0.05	0.02			
P06576	ATP synthase subunit beta, mitochondrial	30	1198	-0.01	0.02	-0.01			
O75947	ATP synthase subunit d, mitochondrial	9	75	-0.01	-0.06	0.24			
P30049	ATP synthase subunit delta, mitochondrial	4	60	-0.02	-0.05	0.21			
P56385	ATP synthase subunit e, mitochondrial	5	105	-0.06	0.09	-0.02			
P56381	ATP synthase subunit epsilon, mitochondrial	2	9	0.23	-0.01	-0.03			
P56134	ATP synthase subunit f, mitochondrial	2	6	0.64	0.44	-0.19			
O75964	ATP synthase subunit g, mitochondrial	7	95	0.08	0.05	-0.08			
P36542	ATP synthase subunit gamma, mitochondrial	12	73	0.22	0.13	-0.16			
P48047	ATP synthase subunit O, mitochondrial	17	172	-0.03	0.02	-0.02			
Q99766	ATP synthase subunit s, mitochondrial	1	2	0.25	0.05	-0.19			
P18859	ATP synthase-coupling factor 6, mitochondrial	5	50	-0.05	0.09	0.20			
O43681	ATPase ASNA1	9	39	-0.11	0.04	0.09			
Q8NBU5	ATPase family AAA domain-containing protein 1	4	9	-0.12	-0.26	-0.01			
Q9ULI0	ATPase family AAA domain-containing protein 2B	1	2	-1.08	-0.22	0.87			
Q9NV17	ATPase family AAA domain-containing protein 3A	7	52	0.15	0.19	0.21			
Q5T9A4	ATPase family AAA domain-containing protein 3B	1	17	-0.34	-0.05	0.30			
Q5T2N8	ATPase family AAA domain-containing protein 3C	1	22	-0.03	0.07	0.11			
Q9UII2	ATPase inhibitor, mitochondrial	6	42	0.04	-0.03	-0.15			
Q96S55	ATPase WRNIP1	3	12	-0.14	-0.37	-0.21			
Q8IZY2	ATP-binding cassette sub-family A member 7	1	1	0.29	0.20	-0.08			
O75027	ATP-binding cassette sub-family B member 7, mitochondrial	1	4	-0.13	-0.02	-0.17			
Q9NUT2	ATP-binding cassette sub-family B member 8, mitochondrial	2	22	0.11	0.15	0.18			
P33897	ATP-binding cassette sub-family D member 1	1	5	0.33	0.61	0.31		4	
Q9UBJ2	ATP-binding cassette sub-family D member 2	1	1	NA	NA	NA			
P61221	ATP-binding cassette sub-family E member 1	17	79	0.50	-0.18	-0.50			5
Q8NE71	ATP-binding cassette sub-family F member 1	26	119	0.04	-0.21	-0.21			
Q9UG63	ATP-binding cassette sub-family F member 2	9	22	0.52	0.14	-0.39			
Q9NUQ8	ATP-binding cassette sub-family F member 3	8	32	0.18	0.04	-0.24			
P53396	ATP-citrate synthase	29	163	-0.07	0.26	0.19			
Q8IW45	ATP-dependent (S)-NAD(P)H-hydrate dehydratase	7	13	0.21	-0.23	-0.43			
O76031	ATP-dependent Clp protease ATP-binding subunit clpX-like, mitochondrial	5	10	0.12	-0.02	-0.10			
P46063	ATP-dependent DNA helicase Q1	20	113	-0.08	0.13	0.26			
Q08211	ATP-dependent RNA helicase A	44	310	0.06	-0.08	-0.16			
Q92499	ATP-dependent RNA helicase DDX1	20	91	0.22	-0.22	-0.44			
Q9NVP1	ATP-dependent RNA helicase DDX18	14	36	0.45	-0.17	-0.53			5
Q9UMR2	ATP-dependent RNA helicase DDX19B	13	84	-0.16	-0.09	0.01			
Q9GZR7	ATP-dependent RNA helicase DDX24	22	111	-0.06	-0.44	-0.40		5	5
O00148	ATP-dependent RNA helicase DDX39A	3	113	-0.29	-0.11	0.06			
O00571	ATP-dependent RNA helicase DDX3X	7	205	-0.08	0.04	0.04			
O15523	ATP-dependent RNA helicase DDX3Y	1	160	-0.13	0.08	0.18			
Q86XP3	ATP-dependent RNA helicase DDX42	21	85	0.04	-0.15	-0.14			
Q9BQ39	ATP-dependent RNA helicase DDX50	5	19	0.15	-0.24	-0.23			

Q8N8A6	ATP-dependent RNA helicase DDX51	7	13	0.27	0.13	-0.11			
Q8TDD1	ATP-dependent RNA helicase DDX54	7	17	0.27	-0.12	-0.29			
Q8NHQ9	ATP-dependent RNA helicase DDX55	4	8	0.04	-0.14	-0.18			
Q7Z478	ATP-dependent RNA helicase DHX29	3	7	0.33	0.25	-0.11			
Q14562	ATP-dependent RNA helicase DHX8	6	18	0.09	-0.07	-0.14			
Q8IYB8	ATP-dependent RNA helicase SUPV3L1, mitochondrial	6	28	0.26	0.06	0.01			
Q96TA2	ATP-dependent zinc metalloprotease YME1L1	4	8	0.10	0.09	0.06			
O14497	AT-rich interactive domain-containing protein 1A	28	105	-0.21	-0.06	0.19			
Q8NFD5	AT-rich interactive domain-containing protein 1B	8	33	-0.14	-0.03	0.04			
Q68CP9	AT-rich interactive domain-containing protein 2	2	4	-0.19	-0.08	0.08			
Q99856	AT-rich interactive domain-containing protein 3A	1	2	-1.55	-0.18	1.36			
Q8IVW6	AT-rich interactive domain-containing protein 3B	3	3	-1.05	-0.69	0.37			
P29374	AT-rich interactive domain-containing protein 4A	5	10	0.05	0.01	-0.06			
Q4LE39	AT-rich interactive domain-containing protein 4B	6	9	-0.02	0.09	0.07			
Q8WXX7	Autism susceptibility gene 2 protein	1	1	NA	NA	NA			
Q9HIY0	Autophagy protein 5	2	3	0.20	-0.07	-0.44			
O75143	Autophagy-related protein 13	1	1	0.20	0.42	0.22			
Q676U5	Autophagy-related protein 16-1	2	8	0.20	0.32	0.11			
Q2TAZ0	Autophagy-related protein 2 homolog A	1	3	0.03	0.08	0.05			
Q96BY7	Autophagy-related protein 2 homolog B	1	2	0.14	0.24	0.11			
Q7Z3C6	Autophagy-related protein 9A	1	1	-0.69	-0.69	0.01			
Q96BJ3	Axin interactor, dorsalization-associated protein	1	1	0.43	0.40	-0.05			
O15169	Axin-1	1	2	-0.24	0.07	0.31			
P20160	Azurocidin	1	4	0.07	0.05	-0.01			
Q13490	Baculoviral IAP repeat-containing protein 2	3	3	-0.40	-0.13	0.32			
Q9NR09	Baculoviral IAP repeat-containing protein 6	3	4	0.03	0.12	0.04			
Q99933	BAG family molecular chaperone regulator 1	5	6	-0.13	-0.09	-0.10			
O95816	BAG family molecular chaperone regulator 2	2	3	-0.45	-0.84	-0.38			
O95817	BAG family molecular chaperone regulator 3	2	5	0.01	-0.23	-0.17			
O95429	BAG family molecular chaperone regulator 4	2	4	-0.93	-0.39	0.54			
Q9UL15	BAG family molecular chaperone regulator 5	3	9	-0.09	-0.12	0.01			
P02730	Band 3 anion transport protein	4	10	-0.87	-0.93	-0.15	3		3
O43491	Band 4.1-like protein 2	4	9	0.28	0.20	-0.06			
Q9Y2J2	Band 4.1-like protein 3	1	5	-0.03	0.33	0.36			
O75531	Barrier-to-autointegration factor	6	58	-0.73	-0.50	0.21	3		4
Q7L1Q6	Basic leucine zipper and W2 domain-containing protein 1	8	28	0.25	0.36	-0.03			
Q9Y6E2	Basic leucine zipper and W2 domain-containing protein 2	1	5	0.35	0.12	-0.22			
P35613	Basigin	3	10	-0.12	0.25	0.39			
Q8WUZ0	B-cell CLL/lymphoma 7 protein family member C	2	3	-0.16	-0.01	0.34			
Q86UU0	B-cell CLL/lymphoma 9-like protein	8	16	-0.13	-0.12	-0.01			
P20749	B-cell lymphoma 3 protein	1	6	-0.01	-0.01	-0.03			
O95999	B-cell lymphoma/leukemia 10	5	6	-0.40	-0.50	-0.03			
Q9C0K0	B-cell lymphoma/leukemia 11B	18	65	0.57	-0.42	-0.71	4		5
Q9UHQ4	B-cell receptor-associated protein 29	1	3	-0.44	0.24	0.68			
P51572	B-cell receptor-associated protein 31	9	62	0.32	0.32	-0.15			
Q92934	Bcl2 antagonist of cell death	2	8	-0.10	0.58	0.57			4
Q16611	Bcl-2 homologous antagonist/killer	1	1	-0.35	0.05	0.41			
Q9NYF8	Bcl-2-associated transcription factor 1	21	123	0.04	-0.16	-0.03			
Q9BXH1	Bcl-2-binding component 3	1	2	NA	NA	NA			
Q14457	Beclin-1	2	5	-0.39	-0.04	0.30			
O15155	BET1 homolog	2	2	0.27	0.42	0.15			
Q9P109	Beta-1,3-galactosyl-O-glycosyl-glycoprotein beta-1,6-N-acetylglucosaminylt	1	2	0.27	-0.27	-0.54			
Q6Y288	Beta-1,3-glucosyltransferase	1	1	-0.41	-0.18	0.23			
Q9UBV7	Beta-1,4-galactosyltransferase 7	1	1	NA	NA	NA			
Q13884	Beta-1-syntrophin	3	13	-0.59	-0.11	0.60			
P02749	Beta-2-glycoprotein 1	1	2	2.42	2.76	0.35			
P61769	Beta-2-microglobulin	4	16	0.01	0.27	0.27			
Q13425	Beta-2-syntrophin	4	13	-0.32	0.67	0.63			4
Q562R1	Beta-actin-like protein 2	1	918	-0.29	-0.04	0.25			
P25098	Beta-adrenergic receptor kinase 1	14	45	-0.11	0.10	0.07			
P49407	Beta-arrestin-1	9	38	-0.81	-0.51	0.59	4		4
P32121	Beta-arrestin-2	6	24	0.13	0.08	-0.35			
Q8WYA6	Beta-catenin-like protein 1	4	9	-0.05	0.05	0.04			
P42025	Beta-centractin	2	48	0.20	-0.11	-0.31			
P13929	Beta-enolase	1	158	-0.25	-0.45	-0.20			
P16278	Beta-galactosidase	6	32	0.10	0.68	0.47			5
P08236	Beta-glucuronidase	1	3	0.19	0.02	-0.15			
P06865	Beta-hexosaminidase subunit alpha	4	20	-0.27	0.40	0.64			
P07686	Beta-hexosaminidase subunit beta	18	69	0.01	0.79	0.58			5
Q53H82	Beta-lactamase-like protein 2	2	2	0.41	0.09	-0.33			
O00462	Beta-mannosidase	2	8	-0.31	0.47	0.73			
Q9HBI1	Beta-parvin	2	3	-0.08	-0.15	-0.07			
P55957	BH3-interacting domain death agonist	5	29	0.33	-0.17	-0.18			
O43252	Bifunctional 3'-phosphoadenosine 5'-phosphosulfate synthase 1	4	5	0.05	0.06	0.57			
Q3LXA3	Bifunctional ATP-dependent dihydroxyacetone kinase/FAD-AMP lyase (cycliz	16	120	-0.08	-0.07	0.01			
Q13057	Bifunctional coenzyme A synthase	5	18	0.07	-0.08	-0.35			
P34913	Bifunctional epoxide hydrolase 2	8	41	0.16	-1.42	-1.64			5
P07814	Bifunctional glutamate/proline--tRNA ligase	45	244	0.31	0.11	-0.14			
Q8IU8	Bifunctional lysine-specific demethylase and histidyl-hydroxylase MINA	3	6	0.38	-0.18	-0.55			
Q9H6W3	Bifunctional lysine-specific demethylase and histidyl-hydroxylase NO66	8	15	0.52	0.17	-0.28			
Q96T60	Bifunctional polynucleotide phosphatase/kinase	12	37	-0.07	0.34	0.38			
O60502	Bifunctional protein NCOAT	8	14	0.05	0.40	0.32			
P31939	Bifunctional purine biosynthesis protein PURH	35	315	0.54	-0.13	-0.64	5		5
Q9Y223	Bifunctional UDP-N-acetylglucosamine 2-epimerase/N-acetylmannosamine	3	6	-0.14	-0.04	0.10			
P53004	Biliverdin reductase A	9	34	-0.23	-0.14	0.12			
P78537	Biogenesis of lysosome-related organelles complex 1 subunit 1	2	8	-0.39	-0.09	0.21			

Q6QNY1	Biogenesis of lysosome-related organelles complex 1 subunit 2	1	1	-0.69	-0.36	0.34			
Q6QNY0	Biogenesis of lysosome-related organelles complex 1 subunit 3	3	17	-0.01	0.08	0.22			
Q9NUP1	Biogenesis of lysosome-related organelles complex 1 subunit 4	3	7	-0.07	0.04	-0.13			
Q8TDH9	Biogenesis of lysosome-related organelles complex 1 subunit 5	3	6	-0.39	-0.20	0.24			
Q8NFC6	Biorientation of chromosomes in cell division protein 1-like 1	24	73	-0.24	-0.19	0.02			
P50747	Biotin--protein ligase	1	1	-0.32	-0.25	0.06			
P49789	Bis(5'-adenosyl)-triphosphatase	1	1	-0.33	-0.57	-0.22			
Q9Y6X5	Bis(5'-adenosyl)-triphosphatase ENPP4	7	18	-0.84	0.09	0.92	4		4
P50583	Bis(5'-nucleosyl)-tetrakisphosphatase	1	1	0.40	0.18	-0.21			
P07738	Bisphosphoglycerate mutase	4	12	-0.47	-0.20	0.13			
Q13867	Bleomycin hydrolase	7	19	0.32	0.18	0.03			
P54132	Bloom syndrome protein	1	5	1.20	0.31	-0.89			
Q9H3K6	BoLA-like protein 2	6	69	0.10	-0.11	-0.17			
Q10589	Bone marrow stromal antigen 2	2	5	-0.50	0.38	0.89			
P80723	Brain acid soluble protein 1	5	15	0.09	0.17	0.09			
O15382	Branched-chain-amino-acid aminotransferase, mitochondrial	4	10	0.20	0.08	-0.14			
Q6UWZ7	BRCA1-A complex subunit Abraxas	3	6	0.22	-0.05	-0.20			
Q9NXR7	BRCA1-A complex subunit BRE	2	2	0.24	0.17	-0.06			
Q96RL1	BRCA1-A complex subunit RAP80	4	12	0.01	-0.14	-0.15			
Q6PJG6	BRCA1-associated ATM activator 1	1	2	-0.36	-0.19	0.16			
Q7Z569	BRCA1-associated protein	1	1	-1.29	-1.70	-0.39			
Q9P287	BRCA2 and CDKN1A-interacting protein	5	6	-0.14	-0.20	-0.12			
P11274	Breakpoint cluster region protein	10	29	-0.33	-0.14	0.28			
Q9HCU9	Breast cancer metastasis-suppressor 1	1	1	-0.30	-0.08	0.22			
Q9H6U6	Breast carcinoma-amplified sequence 3	6	18	0.00	0.20	0.19			
Q9Y6D6	Brefeldin A-inhibited guanine nucleotide-exchange protein 1	4	12	0.00	0.05	0.13			
Q9Y6D5	Brefeldin A-inhibited guanine nucleotide-exchange protein 2	2	6	0.47	0.32	-0.23			
Q9UBW5	Bridging integrator 2	28	189	-0.52	0.12	0.60	4		5
Q9NQY0	Bridging integrator 3	1	1	0.06	0.12	0.06			
Q9NWW8	BRISC and BRCA1-A complex member 1	9	52	-0.09	-0.20	-0.08			
Q15018	BRISC complex subunit Abro1	14	35	0.09	0.05	-0.04			
Q5VW32	BRO1 domain-containing protein BROX	4	9	-0.10	0.16	0.25			
Q8TBE0	Bromo adjacent homology domain-containing 1 protein	1	1	NA	NA	NA			
Q9NRL2	Bromodomain adjacent to zinc finger domain protein 1A	6	10	-0.38	-0.33	-0.01			
Q9UIF9	Bromodomain adjacent to zinc finger domain protein 2A	4	6	-0.19	-0.17	0.11			
Q9ULD4	Bromodomain and PHD finger-containing protein 3	1	2	NA	NA	NA			
Q95696	Bromodomain-containing protein 1	4	7	0.40	0.22	-0.30			
P25440	Bromodomain-containing protein 2	3	8	-0.28	-0.17	0.12			
Q15059	Bromodomain-containing protein 3	5	24	-0.15	-0.14	0.05			
O60885	Bromodomain-containing protein 4	10	44	-0.02	-0.02	-0.02			
Q9NP11	Bromodomain-containing protein 7	2	3	-0.54	-0.20	0.33			
Q9H0E9	Bromodomain-containing protein 8	4	5	0.05	-0.08	-0.04			
Q9NW68	BSD domain-containing protein 1	1	1	0.33	0.28	-0.07			
Q96CX2	BTB/POZ domain-containing protein KCTD12	5	9	-0.09	-0.47	-0.40			
Q96S11	BTB/POZ domain-containing protein KCTD15	1	1	NA	NA	NA			
Q6P147	BTB/POZ domain-containing protein KCTD18	1	1	-0.40	-0.20	0.18			
Q9BRD0	BUD13 homolog	4	6	-0.82	-0.08	0.73			
O00481	Butyrophilin subfamily 3 member A1	1	11	-0.12	0.08	0.30			
P78410	Butyrophilin subfamily 3 member A2	1	11	0.15	0.26	0.11			
O00478	Butyrophilin subfamily 3 member A3	4	16	0.05	0.12	-0.02			
Q6UXG8	Butyrophilin-like protein 9	1	1	-0.84	-1.23	-0.38			
Q13895	Bystin	5	25	0.01	-0.02	-0.09			
P11586	C-1-tetrahydrofolate synthase, cytoplasmic	34	159	0.12	-0.03	-0.14			
O14523	C2 domain-containing protein 2-like	1	1	-1.02	-0.87	0.16			
Q4AC94	C2 domain-containing protein 3	1	3	0.68	0.98	0.31			
Q86Y57	C2 domain-containing protein 5	7	14	0.13	0.01	-0.05			
P21730	C5a anaphylatoxin chemotactic receptor 1	2	2	0.23	-0.02	-0.25			
O75844	CAAX prenyl protease 1 homolog	5	14	0.04	0.17	0.24			
Q8WUQ7	Cactin	6	12	-0.04	0.08	-0.07			
P27708	CAD protein	31	96	0.41	0.02	-0.34			
Q6ZTQ4	Cadherin-related family member 3	1	2	NA	NA	NA			
Q99653	Calcineurin B homologous protein 1	2	2	0.41	0.32	-0.09			
Q9Y6J0	Calcineurin-binding protein cabin-1	5	9	-0.08	-0.01	-0.04			
Q99828	Calcium and integrin-binding protein 1	4	19	-0.24	0.44	0.63			4
Q8IWX8	Calcium homeostasis endoplasmic reticulum protein	9	14	0.06	0.14	0.01			
Q96D31	Calcium release-activated calcium channel protein 1	1	2	0.21	0.43	0.22			
P49069	Calcium signal-modulating cyclophilin ligand	2	2	-0.08	-0.04	0.05			
Q8NE86	Calcium uniporter protein, mitochondrial	1	1	0.18	-1.19	-1.35			
Q9BPX6	Calcium uptake protein 1, mitochondrial	1	3	0.31	0.11	-0.20			
Q8IU85	Calcium/calmodulin-dependent protein kinase type 1D	7	12	0.19	0.30	0.09			
Q13557	Calcium/calmodulin-dependent protein kinase type II subunit delta	8	55	0.42	0.52	0.06			5
Q13555	Calcium/calmodulin-dependent protein kinase type II subunit gamma	6	29	-0.09	-0.11	0.02			
Q16566	Calcium/calmodulin-dependent protein kinase type IV	14	43	0.96	-0.23	-1.03	4		5
Q9P1Z2	Calcium-binding and coiled-coil domain-containing protein 1	2	2	-0.26	0.03	0.29			
O75746	Calcium-binding mitochondrial carrier protein Aralar1	10	38	0.18	0.08	-0.15			
Q6NUK1	Calcium-binding mitochondrial carrier protein SCAAC-1	15	72	0.83	0.56	-0.22	4		4
Q9Y376	Calcium-binding protein 39	7	16	0.39	-0.09	-0.49			
Q9NP80	Calcium-independent phospholipase A2-gamma	1	2	NA	NA	NA			
Q9Y2V2	Calcium-regulated heat stable protein 1	2	13	-1.18	-0.35	1.01	4		4
Q9HB71	Calcyclin-binding protein	9	21	0.47	-0.12	-0.35			
Q9BXY5	Calcyphosin-2	1	1	0.49	0.00	-0.51			
Q05682	Caldesmon	7	14	-0.18	-0.19	-0.10			
P62158	Calmodulin	8	201	0.00	-0.06	0.09			
Q9NZT1	Calmodulin-like protein 5	2	2	1.28	1.29	0.01			
Q7Z624	Calmodulin-lysine N-methyltransferase	1	1	0.21	-0.23	-0.44			
Q9P1Y5	Calmodulin-regulated spectrin-associated protein 3	1	1	-0.29	-0.20	0.08			

P27824	Calnexin	12	69	0.17	0.61	0.51		3	5
P04632	Calpain small subunit 1	9	59	0.25	0.41	0.05			
P07384	Calpain-1 catalytic subunit	11	55	-0.28	0.08	0.35			
O75808	Calpain-15	2	5	-0.62	0.03	0.66			4
P17655	Calpain-2 catalytic subunit	17	99	0.64	0.63	0.21	3	5	
Q9Y6W3	Calpain-7	4	8	0.17	-0.01	-0.10			
P20810	Calpastatin	24	144	0.08	0.60	0.64		3	3
Q99439	Calponin-2	16	332	0.42	0.04	-0.45			
Q15417	Calponin-3	3	20	-0.41	-0.87	-0.46			
P27797	Calreticulin	16	123	-0.02	0.16	0.26			
P17612	cAMP-dependent protein kinase catalytic subunit alpha	2	22	-0.35	-0.32	-0.10			
P22694	cAMP-dependent protein kinase catalytic subunit beta	2	23	-0.53	-0.82	-0.08		3	
P61925	cAMP-dependent protein kinase inhibitor alpha	1	1	-0.09	-1.27	-1.20			
P10644	cAMP-dependent protein kinase type I-alpha regulatory subunit	16	108	-0.57	-0.75	-0.21	4	5	
P31321	cAMP-dependent protein kinase type I-beta regulatory subunit	2	32	-0.19	-0.99	-0.75		4	4
P13861	cAMP-dependent protein kinase type II-alpha regulatory subunit	17	92	0.06	0.00	-0.09			
P56211	cAMP-regulated phosphoprotein 19	1	38	0.49	0.15	-0.26			
Q03060	cAMP-responsive element modulator	1	1	0.65	0.62	-0.02			
O60519	cAMP-responsive element-binding protein-like 2	1	1	0.28	-0.36	-0.64			
Q9BSD7	Cancer-related nucleoside-triphosphatase	7	47	0.00	-0.38	-0.37			
P30622	CAP-Gly domain-containing linker protein 1	18	42	0.00	0.17	0.18			
Q9UDT6	CAP-Gly domain-containing linker protein 2	2	3	-0.14	0.44	0.32			
Q14444	Caprin-1	9	42	0.03	0.07	0.12			
Q8N1G2	Cap-specific mRNA (nucleoside-2'-O-)-methyltransferase 1	5	11	-0.29	0.02	0.31			
Q81YT2	Cap-specific mRNA (nucleoside-2'-O-)-methyltransferase 2	1	1	-0.23	-0.15	0.09			
Q6JBY9	CapZ-interacting protein	17	118	0.00	-0.04	0.02			
Q8IV04	Carabin	8	37	-0.62	-0.15	0.47			
P31327	Carbamoyl-phosphate synthase, mitochondrial	2	5	NA	0.46	NA			
P00915	Carbonic anhydrase 1	7	40	-0.45	-0.41	-0.14			
P00918	Carbonic anhydrase 2	8	29	1.16	1.08	-0.19	5	5	
Q9Y2D0	Carbonic anhydrase 5B, mitochondrial	4	6	-0.31	-0.37	-0.06			
P16152	Carbonyl reductase 1	15	149	-0.17	-0.56	-0.36		5	
O75828	Carbonyl reductase 3	8	68	-0.36	-2.23	-1.88		5	5
Q8N4T8	Carbonyl reductase family member 4	5	18	0.40	-0.23	-0.59			
P48052	Carboxypeptidase A2	1	1	-0.92	-0.10	0.80			
P43155	Carnitine O-acetyltransferase	9	24	0.42	0.37	0.00			
P50416	Carnitine O-palmitoyltransferase 1, liver isoform	4	32	-0.51	0.34	0.87			3
P23786	Carnitine O-palmitoyltransferase 2, mitochondrial	6	15	-0.11	-0.09	0.13			
A5YM72	Carnosine synthase 1	1	1	-1.01	-0.63	0.38			
P49747	Cartilage oligomeric matrix protein	1	2	0.96	1.07	0.12			
P48729	Casein kinase I isoform alpha	2	8	-0.14	0.03	0.18			
P48730	Casein kinase I isoform delta	2	2	0.01	0.44	0.42			
P49674	Casein kinase I isoform epsilon	1	2	0.11	0.14	0.03			
P78368	Casein kinase I isoform gamma-2	1	2	-0.17	-0.09	0.09			
P68400	Casein kinase II subunit alpha	9	41	0.08	0.03	-0.06			
P19784	Casein kinase II subunit alpha'	5	12	-0.16	0.15	0.31			
P67870	Casein kinase II subunit beta	5	24	0.08	0.01	-0.04			
Q9H078	Caseinolytic peptidase B protein homolog	2	5	0.07	0.18	0.11			
Q9H8G2	Caspase activity and apoptosis inhibitor 1	1	2	-0.82	-0.28	0.55			
Q9BXL7	Caspase recruitment domain-containing protein 11	15	41	0.06	0.26	0.17			
Q5EG05	Caspase recruitment domain-containing protein 16	1	29	-0.24	0.28	0.32			
Q9Y2G2	Caspase recruitment domain-containing protein 8	5	11	0.13	0.27	0.25			
P29466	Caspase-1	10	65	1.17	1.04	0.15	5	5	
Q92851	Caspase-10	4	7	-0.89	-0.08	0.55	3		
P31944	Caspase-14	6	7	0.33	0.83	-0.04		3	
P42574	Caspase-3	2	22	-0.77	0.20	0.75	5		5
P49662	Caspase-4	3	14	0.05	0.23	0.18			
P55210	Caspase-7	2	10	-0.05	0.10	0.05			
Q14790	Caspase-8	5	19	-0.21	0.26	0.45			
P55211	Caspase-9	1	1	-0.72	0.07	0.78			
Q9BXW7	Cat eye syndrome critical region protein 5	9	38	0.47	0.00	-0.51			
P04040	Catalase	16	66	-0.20	-0.21	0.05			
P21964	Catechol O-methyltransferase	2	10	-0.20	-0.08	0.18			
P07858	Cathepsin B	3	13	0.60	-0.02	-0.47			
P07339	Cathepsin D	18	223	-1.04	0.10	1.21	4		4
P08311	Cathepsin G	4	17	0.12	-0.02	-0.37			
P25774	Cathepsin S	7	18	-0.13	0.53	0.46		4	5
P56202	Cathepsin W	4	24	-0.41	0.89	1.61		5	5
Q9UBR2	Cathepsin Z	3	27	-0.49	0.69	0.87		5	5
P20645	Cation-dependent mannose-6-phosphate receptor	4	11	0.00	-0.07	0.04			
P11717	Cation-independent mannose-6-phosphate receptor	19	47	-0.71	0.37	1.01	4		5
P51681	C-C chemokine receptor type 5	1	1	1.45	1.80	0.33			
P13501	C-C motif chemokine 5	6	12	-1.49	-0.44	1.27	4		4
Q96Q11	CCA tRNA nucleotidyltransferase 1, mitochondrial	10	26	-0.08	-0.38	-0.36			
P17676	CCAAT/enhancer-binding protein beta	1	1	NA	NA	NA			
Q03701	CCAAT/enhancer-binding protein zeta	2	3	0.53	0.31	-0.22			
A5YKK6	CCR4-NOT transcription complex subunit 1	14	30	0.10	0.11	0.01			
Q9H9A5	CCR4-NOT transcription complex subunit 10	2	3	-0.34	0.10	0.30			
Q9UKZ1	CCR4-NOT transcription complex subunit 11	2	8	0.00	0.02	-0.05			
Q9NZN8	CCR4-NOT transcription complex subunit 2	7	32	-0.13	-0.06	0.12			
O75175	CCR4-NOT transcription complex subunit 3	6	18	-0.20	-0.28	-0.10			
Q96L15	CCR4-NOT transcription complex subunit 6-like	3	4	0.23	0.00	-0.23			
Q9UIV1	CCR4-NOT transcription complex subunit 7	2	3	-0.16	-0.05	0.10			
O95971	CD160 antigen	1	2	-1.27	0.15	1.42			
O95400	CD2 antigen cytoplasmic tail-binding protein 2	7	18	-0.49	-0.20	0.19			
Q9Y5K6	CD2-associated protein	19	61	0.16	0.00	-0.17			

P16070	CD44 antigen	9	126	0.72	0.65	-0.18	4	5
P09326	CD48 antigen	6	39	0.76	0.78	0.06	5	5
P13987	CD59 glycoprotein	2	13	0.75	0.50	-0.23	5	5
P60033	CD81 antigen	1	4	0.47	0.45	-0.02		
P27701	CD82 antigen	1	1	0.46	0.77	0.32		
P21926	CD9 antigen	1	8	0.23	-0.31	-0.48		
P48960	CD97 antigen	5	46	-0.47	0.49	0.92		5
P14209	CD99 antigen	4	28	-0.01	0.34	0.85		
Q9NRR8	CDC42 small effector protein 1	1	1	-0.91	0.45	1.38		
Q9NRR3	CDC42 small effector protein 2	3	24	0.22	0.07	-0.12		
Q15642	Cdc42-interacting protein 4	1	1	-0.04	0.81	0.85		
Q9NZ45	CDGSH iron-sulfur domain-containing protein 1	4	11	0.25	-0.12	-0.34		
Q8N5K1	CDGSH iron-sulfur domain-containing protein 2	4	10	0.37	0.45	0.18		
P0C7P0	CDGSH iron-sulfur domain-containing protein 3, mitochondrial	5	9	-0.44	0.46	0.77		
Q96S26	CDK5 regulatory subunit-associated protein 1	1	2	NA	NA	NA		
Q96SN8	CDK5 regulatory subunit-associated protein 2	1	5	-0.97	-1.17	-0.19		
Q96JB5	CDK5 regulatory subunit-associated protein 3	7	36	0.53	0.08	-0.27		
P51948	CDK-activating kinase assembly factor MAT1	1	1	-1.02	-0.88	0.16		
Q9NXV6	CDKN2A-interacting protein	19	81	-0.16	-0.32	-0.16		
Q96HQ2	CDKN2AIP N-terminal-like protein	2	4	-0.50	0.08	0.58		
Q32N88	CDP-diacylglycerol--glycerol 3-phosphate 3-phosphatidyltransferase, mitoch	1	1	-0.02	-0.02	0.01		
O14735	CDP-diacylglycerol--inositol 3-phosphatidyltransferase	1	4	NA	NA	NA		
Q8N163	Cell cycle and apoptosis regulator protein 2	26	158	-0.07	-0.13	-0.01		
Q99638	Cell cycle checkpoint control protein RAD9A	1	1	-0.28	-0.22	0.06		
Q9NV96	Cell cycle control protein 50A	1	5	-1.07	0.15	1.23		
Q9NQS1	Cell death regulator Aven	1	2	-0.10	0.11	0.21		
Q92600	Cell differentiation protein RCD1 homolog	4	14	-0.09	-0.05	0.03		
P60953	Cell division control protein 42 homolog	9	108	0.04	0.15	0.27		
Q99459	Cell division cycle 5-like protein	28	131	-0.11	-0.09	0.02		
Q8IX12	Cell division cycle and apoptosis regulator protein 1	21	88	-0.07	-0.11	-0.03		
P30260	Cell division cycle protein 27 homolog	3	4	-0.22	0.21	0.16		
Q9NX58	Cell growth-regulating nucleolar protein	15	63	0.33	0.33	0.12		
P62633	Cellular nucleic acid-binding protein	9	43	0.28	-0.07	-0.30		
P41208	Centrin-2	5	10	-0.06	-0.45	-0.32		
O15182	Centrin-3	2	4	-0.20	-0.71	-0.51		
Q6IQ19	Centriole, cilia and spindle-associated protein	1	1	0.62	-0.08	-0.69		
Q7Z7A1	Centriolin	8	19	0.08	-0.20	-0.21		
Q8N137	Centrobin	2	4	-0.12	-0.22	-0.09		
Q03188	Centromere protein C	11	32	-0.37	-0.05	0.33		
Q7Z7K6	Centromere protein V	6	21	0.10	-0.28	-0.40		
O43264	Centromere/kinetochore protein zw10 homolog	1	1	1.56	-0.29	-1.84		
Q02224	Centromere-associated protein E	1	7	0.64	0.19	-0.41		
Q8N960	Centrosomal protein of 120 kDa	4	5	0.00	-0.08	-0.08		
Q66G59	Centrosomal protein of 135 kDa	3	6	-0.19	-0.15	0.04		
Q5SW79	Centrosomal protein of 170 kDa	4	10	0.09	-0.30	-0.20		
Q9BYV8	Centrosomal protein of 41 kDa	1	4	-0.24	-0.17	0.09		
Q86XR8	Centrosomal protein of 57 kDa	4	11	0.12	-0.20	-0.22		
Q8NA72	Centrosomal protein POC5	2	2	-1.18	-0.90	0.28		
Q5VT06	Centrosome-associated protein 350	3	3	-0.08	0.08	0.17		
Q9BV73	Centrosome-associated protein CEP250	19	33	-0.12	-0.12	0.00		
Q9NWW5	Ceroid-lipofuscinosis neuronal protein 6	2	2	-0.13	-0.09	0.05		
Q9UFW8	CGG triplet repeat-binding protein 1	9	38	0.02	0.01	0.13		
Q13370	cGMP-inhibited 3',5'-cyclic phosphodiesterase B	2	2	0.65	0.49	-0.16		
Q8NI60	Chaperone activity of bc1 complex-like, mitochondrial	4	9	-0.04	-0.49	-0.21		
Q9HD42	Charged multivesicular body protein 1a	4	26	-0.07	0.09	0.27		
Q7LBR1	Charged multivesicular body protein 1b	4	21	-0.32	-0.22	0.18		
O43633	Charged multivesicular body protein 2a	7	51	-0.21	-0.06	0.09		
Q9UQN3	Charged multivesicular body protein 2b	5	24	0.36	0.00	-0.33		
Q9Y3E7	Charged multivesicular body protein 3	2	2	-0.06	-0.24	-0.18		
Q9BY43	Charged multivesicular body protein 4a	8	46	-0.07	0.06	0.12		
Q9H444	Charged multivesicular body protein 4b	10	77	-0.20	-0.19	0.04		
Q9NZ23	Charged multivesicular body protein 5	6	23	-0.26	-0.31	0.20		
Q96FZ7	Charged multivesicular body protein 6	4	18	-0.17	0.38	0.50		
Q8WUX9	Charged multivesicular body protein 7	5	12	0.06	-1.07	-1.14	3	3
Q9BWS9	Chitinase domain-containing protein 1	4	7	0.12	0.04	-0.07		
Q9BT22	Chitobiosyldiphosphodolichol beta-mannosyltransferase	2	7	-0.07	0.09	0.16		
Q96S66	Chloride channel CLIC-like protein 1	2	4	0.12	-0.36	-0.35		
O00299	Chloride intracellular channel protein 1	18	289	-0.44	0.84	0.96	4	4
O95833	Chloride intracellular channel protein 3	12	60	-1.89	0.36	1.93	5	5
Q9Y696	Chloride intracellular channel protein 4	1	11	-0.78	-0.12	0.66		
Q9NZA1	Chloride intracellular channel protein 5	2	11	1.43	0.61	-0.82		
Q9Y259	Choline/ethanolamine kinase	4	12	0.01	0.14	-0.02		
P49585	Choline-phosphate cytidyltransferase A	7	24	-0.06	0.27	0.49		4
Q9NRG0	Chromatin accessibility complex protein 1	2	7	-0.18	-0.18	-0.01		
Q8IXM2	Chromatin complexes subunit BAP18	9	92	-0.98	-0.09	0.82	5	5
Q9HAF1	Chromatin modification-related protein MEAF6	3	10	-0.04	-0.08	0.00		
Q9Y3Y2	Chromatin target of PRMT1 protein	5	77	-0.16	-0.24	0.00		
P83916	Chromobox protein homolog 1	7	113	0.03	0.13	0.01		
Q13185	Chromobox protein homolog 3	11	137	-0.44	-0.27	0.19		
P45973	Chromobox protein homolog 5	9	47	-0.14	-0.29	-0.19		
O95503	Chromobox protein homolog 6	2	4	-0.13	0.21	0.19		
Q9HC52	Chromobox protein homolog 8	2	5	-0.27	-0.08	0.20		
Q9Y232	Chromodomain Y-like protein	2	7	-0.26	-0.01	0.26		
O14647	Chromodomain-helicase-DNA-binding protein 2	4	4	-0.02	-0.07	-0.07		
Q12873	Chromodomain-helicase-DNA-binding protein 3	7	32	-0.19	-0.35	-0.18		
Q14839	Chromodomain-helicase-DNA-binding protein 4	20	72	-0.13	-0.04	0.14		

Q9HCK8	Chromodomain-helicase-DNA-binding protein 8	3	23	-0.18	-0.10	0.06			
Q96JM3	Chromosome alignment-maintaining phosphoprotein 1	12	30	-0.11	-0.22	-0.17			
Q8WWB6	Chromosome transmission fidelity protein 18 homolog	1	1	0.07	0.10	0.03			
P0CG12	Chromosome transmission fidelity protein 8 homolog isoform 2	7	53	-0.40	-0.17	0.22			
Q9ULV3	Cip1-interacting zinc finger protein	6	9	-0.28	-0.19	0.25			
Q8N0X4	Citrate lyase subunit beta-like protein, mitochondrial	8	18	0.27	-0.17	-0.43			
Q75390	Citrate synthase, mitochondrial	13	161	0.26	0.13	-0.14			
O60271	C-Jun-amino-terminal kinase-interacting protein 4	10	12	-0.06	-0.02	0.11			
Q9NX76	CKLF-like MARVEL transmembrane domain-containing protein 6	1	1	0.74	0.68	-0.06			
Q00610	Clathrin heavy chain 1	52	293	-0.17	0.25	0.35			
Q8NHS4	Clathrin heavy chain linker domain-containing protein 1	1	1	0.42	0.13	-0.27			
Q14677	Clathrin interactor 1	10	32	-0.29	0.17	0.28			
P09496	Clathrin light chain A	6	22	-0.67	0.35	1.03			
P09497	Clathrin light chain B	5	32	-0.28	0.11	0.43			
Q10570	Cleavage and polyadenylation specificity factor subunit 1	14	26	0.04	-0.17	-0.11			
Q9P210	Cleavage and polyadenylation specificity factor subunit 2	8	17	-0.15	-0.17	-0.03			
Q9UKF6	Cleavage and polyadenylation specificity factor subunit 3	7	19	-0.04	-0.15	-0.12			
O95639	Cleavage and polyadenylation specificity factor subunit 4	4	6	0.00	-0.04	0.04			
O43809	Cleavage and polyadenylation specificity factor subunit 5	11	49	-0.17	-0.18	-0.21			
Q16630	Cleavage and polyadenylation specificity factor subunit 6	6	36	0.01	-0.03	-0.06			
Q8N684	Cleavage and polyadenylation specificity factor subunit 7	11	80	-0.17	-0.19	-0.02			
Q05048	Cleavage stimulation factor subunit 1	9	28	-0.03	-0.07	-0.07			
P33240	Cleavage stimulation factor subunit 2	6	71	-0.16	-0.17	-0.01			
Q9H0L4	Cleavage stimulation factor subunit 2 tau variant	9	53	-0.20	-0.25	0.00			
Q12996	Cleavage stimulation factor subunit 3	6	9	0.10	-0.39	-0.32			
O96005	Cleft lip and palate transmembrane protein 1	3	3	0.17	0.27	0.10			
Q7Z460	CLIP-associating protein 1	10	24	0.06	0.13	0.42			
O75122	CLIP-associating protein 2	10	28	-0.14	0.13	0.34			
P10909	Clusterin	3	3	0.07	-0.48	-0.57			
Q9UGN4	CMRF35-like molecule 8	3	3	-1.81	-0.57	1.25			
Q7Z401	C-myc promoter-binding protein	1	3	-0.28	-0.28	0.01			
Q99417	C-Myc-binding protein	4	21	-0.19	0.01	0.19			
Q14019	Coactosin-like protein	13	156	-0.24	-1.53	-1.79	5		5
P12259	Coagulation factor V	2	2	0.94	1.07	0.13			
P00488	Coagulation factor XIII A chain	9	28	-0.13	-0.28	-0.02			
P53621	Coatomer subunit alpha	29	139	0.17	0.28	0.16			
P53618	Coatomer subunit beta	16	86	0.10	0.27	0.19			
P35606	Coatomer subunit beta'	16	48	0.13	0.34	0.08			
P48444	Coatomer subunit delta	23	107	0.08	0.23	0.20			
O14579	Coatomer subunit epsilon	10	38	0.25	0.20	0.10			
Q9Y678	Coatomer subunit gamma-1	19	110	0.10	0.47	0.40	5		
Q9UBF2	Coatomer subunit gamma-2	4	18	0.01	-0.12	-0.04			
P61923	Coatomer subunit zeta-1	3	41	0.05	0.10	0.11			
Q96EY8	Cob(II)yrinic acid a,c-diamide adenosyltransferase, mitochondrial	1	3	-0.97	-0.46	0.51			
O00748	Cocaine esterase	1	2	-3.43	0.18	3.63			
Q8IWY9	Codanin-1	1	1	0.36	0.13	-0.23			
P23528	Cofilin-1	15	605	-0.49	-0.24	0.37	5		
Q9Y281	Cofilin-2	2	206	-0.12	0.10	0.22			
Q8WVM7	Cohesin subunit SA-1	5	12	-0.04	-0.11	0.14			
Q8N3U4	Cohesin subunit SA-2	5	20	-0.09	0.04	0.21			
Q6P1N0	Coiled-coil and C2 domain-containing protein 1A	9	13	-0.26	0.14	0.44			
Q5T0F9	Coiled-coil and C2 domain-containing protein 1B	7	18	-0.27	-0.09	0.31			
Q96A19	Coiled-coil domain-containing protein 102A	3	6	-0.32	0.03	0.48			
Q96NT0	Coiled-coil domain-containing protein 115	1	1	-0.13	-0.09	0.02			
Q81WD4	Coiled-coil domain-containing protein 117	1	2	-1.36	-0.38	0.98			
Q8WUD4	Coiled-coil domain-containing protein 12	5	30	-0.23	-0.17	0.18			
Q96CT7	Coiled-coil domain-containing protein 124	6	21	0.22	-0.09	-0.21			
Q96BQ5	Coiled-coil domain-containing protein 127	1	2	-0.10	-0.11	-0.01			
Q96JG6	Coiled-coil domain-containing protein 132	4	4	-0.11	0.05	0.08			
Q9H6E4	Coiled-coil domain-containing protein 134	2	2	-0.01	0.17	0.17			
Q6PK04	Coiled-coil domain-containing protein 137	3	8	-0.15	0.00	0.08			
Q8NCX0	Coiled-coil domain-containing protein 150	1	5	-0.19	-0.35	-0.15			
Q6TFL3	Coiled-coil domain-containing protein 171	1	1	0.16	0.33	0.17			
Q9P1Z9	Coiled-coil domain-containing protein 180	1	7	NA	NA	NA			
O60826	Coiled-coil domain-containing protein 22	7	12	-0.13	-0.02	0.20			
Q86WR0	Coiled-coil domain-containing protein 25	2	3	0.23	-0.06	-0.31			
Q81WP9	Coiled-coil domain-containing protein 28A	1	4	-0.03	-0.06	-0.02			
Q96M95	Coiled-coil domain-containing protein 42A	1	1	0.32	-0.47	-0.79			
Q96MW1	Coiled-coil domain-containing protein 43	2	14	0.03	0.05	-0.05			
Q96A33	Coiled-coil domain-containing protein 47	4	5	0.18	0.21	0.10			
Q81VM0	Coiled-coil domain-containing protein 50	1	4	-1.19	-0.09	1.09	4		4
Q96ER9	Coiled-coil domain-containing protein 51	1	7	0.22	0.02	-0.20			
Q4VC31	Coiled-coil domain-containing protein 58	4	16	0.17	-0.07	-0.39			
Q16204	Coiled-coil domain-containing protein 6	9	23	-0.14	0.15	0.25			
A2IDD5	Coiled-coil domain-containing protein 78	1	1	NA	NA	NA			
Q8N4S0	Coiled-coil domain-containing protein 82	1	1	-1.96	-1.39	0.58			
Q9H6F5	Coiled-coil domain-containing protein 86	9	26	0.30	-0.10	-0.39			
A6NC98	Coiled-coil domain-containing protein 88B	34	88	-0.41	0.09	0.71			5
Q9Y3X0	Coiled-coil domain-containing protein 9	6	28	-0.05	-0.03	0.04			
Q9GZT6	Coiled-coil domain-containing protein 90B, mitochondrial	3	5	0.03	-0.10	-0.24			
Q7Z6B0	Coiled-coil domain-containing protein 91	3	5	0.32	-0.01	-0.32			
Q567U6	Coiled-coil domain-containing protein 93	6	9	-0.01	0.07	0.20			
Q9BW85	Coiled-coil domain-containing protein 94	3	9	-0.06	-0.01	0.13			
Q96F63	Coiled-coil domain-containing protein 97	1	2	0.18	0.14	-0.03			
Q96BP2	Coiled-coil-helix-coiled-coil-helix domain-containing protein 1	1	1	0.10	0.03	-0.09			
Q9NX63	Coiled-coil-helix-coiled-coil-helix domain-containing protein 3, mitochondrial	13	57	0.04	0.04	-0.01			

Q9BRQ6	Coiled-coil-helix-coiled-coil-helix domain-containing protein 6, mitochondria	3	7	0.32	-0.16	-0.59			
Q9BUK0	Coiled-coil-helix-coiled-coil-helix domain-containing protein 7	1	1	0.63	0.56	-0.06			
P38432	Collin	1	1	-0.11	0.06	0.18			
O75534	Cold shock domain-containing protein E1	10	30	0.04	0.01	-0.09			
Q14011	Cold-inducible RNA-binding protein	5	32	-0.26	-0.07	0.27			
P12109	Collagen alpha-1(VI) chain	1	1	0.80	0.50	-0.29			
P39060	Collagen alpha-1(XVIII) chain	1	3	NA	NA	NA			
P08123	Collagen alpha-2(I) chain	1	2	NA	NA	NA			
Q9Y5P4	Collagen type IV alpha-3-binding protein	1	3	-0.09	0.07	0.19			
P23508	Colorectal mutant cancer protein	1	2	NA	NA	NA			
Q8N668	COMM domain-containing protein 1	1	3	-0.28	0.40	0.68			
Q9UBI1	COMM domain-containing protein 3	2	4	-0.09	-0.07	0.06			
Q7Z4G1	COMM domain-containing protein 6	2	2	-0.71	-0.23	0.49			
Q9NX08	COMM domain-containing protein 8	2	5	-0.19	0.06	0.21			
Q9P000	COMM domain-containing protein 9	2	3	-0.12	-0.77	-0.13			
P01024	Complement C3	1	6	0.96	1.19	0.23			
P0C0L4	Complement C4-A	1	2	-0.41	0.27	0.67			
Q07021	Complement component 1 Q subcomponent-binding protein, mitochondrial	6	24	0.52	0.05	-0.36			
P02748	Complement component C9	1	2	NA	NA	NA			
Q9NPL8	Complex I assembly factor TIMMDC1, mitochondrial	1	2	-0.07	-0.46	-0.38			
Q8IUX1	Complex I assembly factor TMEM126B, mitochondrial	1	1	-0.02	-0.17	-0.15			
Q5U5X0	Complex III assembly factor LYRM7	1	4	0.01	-0.22	0.07			
Q8WTW3	Conserved oligomeric Golgi complex subunit 1	4	5	0.04	0.06	-0.01			
Q14746	Conserved oligomeric Golgi complex subunit 2	3	5	0.01	0.19	0.22			
Q96JB2	Conserved oligomeric Golgi complex subunit 3	1	1	0.25	0.31	0.07			
Q9H9E3	Conserved oligomeric Golgi complex subunit 4	2	2	0.03	0.12	0.09			
Q9UP83	Conserved oligomeric Golgi complex subunit 5	1	2	NA	NA	NA			
Q9Y2V7	Conserved oligomeric Golgi complex subunit 6	2	2	0.01	0.08	0.07			
P83436	Conserved oligomeric Golgi complex subunit 7	2	4	-0.11	0.07	0.18			
Q6PJW8	Consortin	1	1	-0.16	-0.06	0.08			
Q96EK7	Constitutive coactivator of peroxisome proliferator-activated receptor gamma	3	10	-0.09	-0.11	-0.10			
Q9NZB2	Constitutive coactivator of PPAR-gamma-like protein 1	24	61	0.07	0.15	0.16			
Q13098	COP9 signalosome complex subunit 1	7	25	0.17	-0.06	-0.19			
P61201	COP9 signalosome complex subunit 2	6	9	0.28	0.01	-0.30			
Q9UN52	COP9 signalosome complex subunit 3	10	32	0.24	-0.15	-0.17			
Q9BT78	COP9 signalosome complex subunit 4	12	77	0.28	0.01	-0.24			
Q92905	COP9 signalosome complex subunit 5	4	26	0.43	0.17	-0.32			
Q7L5N1	COP9 signalosome complex subunit 6	6	28	0.20	-0.04	-0.27			
Q9UBW8	COP9 signalosome complex subunit 7a	3	4	0.32	0.04	-0.27			
Q9H9Q2	COP9 signalosome complex subunit 7b	3	20	-0.07	-0.12	0.05			
Q99627	COP9 signalosome complex subunit 8	4	27	0.20	0.04	-0.09			
Q99829	Copine-1	13	83	0.14	0.24	0.08			
O75131	Copine-3	12	58	0.17	0.13	-0.03			
O14618	Copper chaperone for superoxide dismutase	6	31	-0.24	-0.34	-0.14			
Q9NTM9	Copper homeostasis protein cutC homolog	7	31	0.04	-0.35	-0.26			
O00244	Copper transport protein ATOX1	5	18	-0.64	0.30	0.84	3		4
Q04656	Copper-transporting ATPase 1	1	2	NA	NA	NA			
P36551	Coproporphyrinogen-III oxidase, mitochondrial	5	17	0.06	0.11	0.07			
O75367	Core histone macro-H2A.1	20	597	0.03	-0.12	-0.11			
Q9P0M6	Core histone macro-H2A.2	1	70	-0.07	-0.01	0.04			
Q13951	Core-binding factor subunit beta	6	39	-0.27	-0.13	0.20			
Q15517	Corneodesmosin	2	2	-0.15	-1.87	-1.74			
P31146	Coronin-1A	24	786	0.01	-0.03	-0.06			
Q9BR76	Coronin-1B	2	3	-0.69	-0.24	0.46			
Q9ULV4	Coronin-1C	6	15	-0.86	-0.06	0.64	5		5
Q92828	Coronin-2A	3	3	0.11	-0.12	-0.30			
P57737	Coronin-7	23	146	0.27	0.25	0.06			
Q9P1F3	Costars family protein ABRACL	1	7	NA	NA	NA			
Q9NRP2	COX assembly mitochondrial protein 2 homolog	1	3	-1.01	-0.26	0.74			
Q7Z7K0	COX assembly mitochondrial protein homolog	1	2	0.21	0.28	0.07			
Q9P0U4	CpG-binding protein	2	5	-0.09	-0.26	-0.17			
Q9UEE9	Craniofacial development protein 1	2	6	0.16	-0.18	-0.34			
Q8IUR6	CREB3 regulatory factor	1	1	0.13	-0.31	-0.42			
Q92793	CREB-binding protein	9	20	-0.10	-0.04	0.14			
Q6UUV9	CREB-regulated transcription coactivator 1	3	3	-1.31	-0.46	0.76			
Q53ET0	CREB-regulated transcription coactivator 2	3	7	-0.07	0.17	0.21			
Q6UUV7	CREB-regulated transcription coactivator 3	4	11	-0.45	-0.40	0.12			
P46109	Crk-like protein	10	66	-0.02	0.19	0.23			
Q9BZJ0	Crooked neck-like protein 1	7	15	-0.04	0.13	0.04			
Q9H668	CST complex subunit STN1	1	1	-0.08	-0.07	0.02			
O15320	cTAGE family member 5	5	8	-0.36	-0.13	-0.03			
Q05D32	CTD small phosphatase-like protein 2	5	19	-0.09	-0.02	0.09			
Q13363	C-terminal-binding protein 1	8	83	-0.28	0.11	0.35			
P56545	C-terminal-binding protein 2	4	29	-1.34	0.05	1.25	3		3
P17812	CTP synthase 1	4	13	-0.29	-0.19	0.07			
Q9NRF8	CTP synthase 2	1	3	0.04	-0.64	-0.69			
Q9Y240	C-type lectin domain family 11 member A	1	1	0.49	0.63	0.14			
Q92478	C-type lectin domain family 2 member B	1	3	-0.59	0.51	1.03			3
Q92879	CUGBP Elav-like family member 1	1	9	0.23	0.04	-0.21			
Q95319	CUGBP Elav-like family member 2	10	68	-0.15	-0.06	0.19			
Q13616	Cullin-1	5	7	-0.11	0.05	0.05			
Q13617	Cullin-2	6	22	0.16	-0.09	-0.18			
Q13618	Cullin-3	8	28	0.19	-0.01	-0.28			
Q13619	Cullin-4A	3	16	0.27	0.18	-0.09			
Q13620	Cullin-4B	5	26	0.28	-0.05	-0.34			
Q93034	Cullin-5	3	6	0.32	0.07	-0.15			

Q86VP6	Cullin-associated NEDD8-dissociated protein 1	32	127	0.22	-0.02	-0.28			
Q69YN2	CWF19-like protein 1	8	14	0.19	-0.16	-0.20			
Q2TBE0	CWF19-like protein 2	2	3	-0.05	0.25	0.31			
Q7LFL8	CXXC-type zinc finger protein 5	1	1	-1.24	0.47	1.72			
P18846	Cyclic AMP-dependent transcription factor ATF-1	1	28	-0.69	-0.16	0.52			
P15336	Cyclic AMP-dependent transcription factor ATF-2	1	6	-0.40	0.02	0.43			
P17544	Cyclic AMP-dependent transcription factor ATF-7	1	1	-1.70	0.10	1.81			
P16220	Cyclic AMP-responsive element-binding protein 1	4	54	-0.26	-0.07	0.00			
Q9UQ88	Cyclin-dependent kinase 11A	6	17	0.11	-0.28	-0.15			
Q9NYV4	Cyclin-dependent kinase 12	5	7	-0.14	-0.29	-0.04			
Q14004	Cyclin-dependent kinase 13	2	3	-0.27	-0.01	0.27			
Q00537	Cyclin-dependent kinase 17	2	3	0.09	0.49	0.50			
Q9BWU1	Cyclin-dependent kinase 19	1	4	-0.32	0.21	0.40			
P24941	Cyclin-dependent kinase 2	4	9	-0.52	-0.29	0.23			
P42773	Cyclin-dependent kinase 4 inhibitor C	4	9	-0.55	0.27	0.51			
Q00535	Cyclin-dependent kinase 5	2	9	-0.22	0.03	0.19			
Q00534	Cyclin-dependent kinase 6	3	16	0.13	0.52	0.52		3	4
P50750	Cyclin-dependent kinase 9	3	21	-0.28	-0.14	0.01			
P46527	Cyclin-dependent kinase inhibitor 1B	7	32	0.11	0.01	-0.03			
O14976	Cyclin-G-associated kinase	17	56	-0.11	0.18	0.26			
O75909	Cyclin-K	1	1	0.30	0.03	-0.26			
Q96S94	Cyclin-L2	1	4	-0.25	-0.16	0.04			
Q60563	Cyclin-T1	4	6	-0.41	-0.35	0.06			
Q8ND76	Cyclin-Y	2	10	0.02	0.03	0.01			
P01040	Cystatin-A	1	1	-0.19	-2.45	-2.27			
P04080	Cystatin-B	5	66	-0.22	-0.02	-0.17			
O76096	Cystatin-F	3	22	-0.63	1.33	1.93	4	5	5
Q15828	Cystatin-M	1	1	0.01	-1.07	-1.10			
P21291	Cysteine and glycine-rich protein 1	7	33	-0.10	0.26	0.17			
Q9UHD1	Cysteine and histidine-rich domain-containing protein 1	8	21	-0.01	-0.25	-0.18			
Q9Y697	Cysteine desulfurase, mitochondrial	8	15	0.20	-0.34	-0.46			
Q9Y4P1	Cysteine protease ATG4B	1	1	-0.13	0.03	0.17			
Q9P021	Cysteine-rich PDZ-binding protein	1	1	0.47	1.15	0.69			
P50238	Cysteine-rich protein 1	4	29	0.47	0.52	-0.02		3	
P52943	Cysteine-rich protein 2	1	13	0.54	0.28	-0.26			
Q6UXH1	Cysteine-rich with EGF-like domain protein 2	1	1	-0.03	0.07	0.11			
P49589	Cysteine--tRNA ligase, cytoplasmic	13	48	0.30	0.18	-0.01			
Q53TN4	Cytochrome b reductase 1	1	2	-1.52	-0.16	1.37			
P04839	Cytochrome b-245 heavy chain	2	4	0.22	0.01	-0.21			
P13498	Cytochrome b-245 light chain	1	2	0.26	0.66	0.40			
P00167	Cytochrome b5	4	22	0.54	0.23	-0.22			
Q7L1T6	Cytochrome b5 reductase 4	1	1	0.03	0.24	0.21			
O43169	Cytochrome b5 type B	1	2	-0.16	0.07	0.23			
O14569	Cytochrome b561 domain-containing protein 2	1	1	0.92	0.93	0.02			
P31930	Cytochrome b-c1 complex subunit 1, mitochondrial	14	139	0.29	0.11	0.09			
P22695	Cytochrome b-c1 complex subunit 2, mitochondrial	22	219	0.07	0.10	0.04			
P07919	Cytochrome b-c1 complex subunit 6, mitochondrial	5	7	-0.71	-0.26	0.12			
P14927	Cytochrome b-c1 complex subunit 7	6	22	-0.12	0.08	0.35			
O14949	Cytochrome b-c1 complex subunit 8	4	21	-0.06	0.02	0.12			
Q9UDW1	Cytochrome b-c1 complex subunit 9	1	3	0.36	0.23	-0.13			
P47985	Cytochrome b-c1 complex subunit Rieske, mitochondrial	9	72	-0.14	0.04	0.17			
P99999	Cytochrome c	10	127	0.10	0.25	0.00			
Q9NYJ1	Cytochrome c oxidase assembly factor 4 homolog, mitochondrial	1	2	0.09	-0.14	-0.24			
Q5JTJ3	Cytochrome c oxidase assembly factor 6 homolog	1	1	-0.12	0.11	0.22			
Q9Y2R0	Cytochrome c oxidase assembly protein 3 homolog, mitochondrial	2	3	0.55	0.29	-0.27			
Q49B96	Cytochrome c oxidase assembly protein COX19	1	4	0.13	0.00	0.00			
Q14061	Cytochrome c oxidase copper chaperone	1	5	0.02	-0.02	0.36			
Q5RI15	Cytochrome c oxidase protein 20 homolog	1	1	0.54	0.35	-0.18			
P00403	Cytochrome c oxidase subunit 2	5	50	0.51	0.29	-0.25			
P13073	Cytochrome c oxidase subunit 4 isoform 1, mitochondrial	6	80	0.33	0.23	-0.09			
P20674	Cytochrome c oxidase subunit 5A, mitochondrial	6	102	-0.08	-0.08	0.11			
P10606	Cytochrome c oxidase subunit 5B, mitochondrial	6	61	0.07	-0.11	-0.10			
P14854	Cytochrome c oxidase subunit 6B1	5	19	0.60	0.27	-0.25			
P09669	Cytochrome c oxidase subunit 6C	2	26	-0.07	-0.13	-0.21			
P14406	Cytochrome c oxidase subunit 7A2, mitochondrial	3	31	0.22	0.01	-0.19			
O14548	Cytochrome c oxidase subunit 7A-related protein, mitochondrial	4	13	-0.02	0.45	0.43			
P15954	Cytochrome c oxidase subunit 7C, mitochondrial	3	28	0.41	0.00	-0.23			
P10176	Cytochrome c oxidase subunit 8A, mitochondrial	1	5	-0.15	-0.39	-0.08			
P08574	Cytochrome c1, heme protein, mitochondrial	3	8	-0.02	-0.12	-0.01			
Q6UW02	Cytochrome P450 20A1	3	7	0.49	0.16	-0.20			
Q15438	Cytohesin-1	4	22	0.23	-0.14	-0.59			
O43739	Cytohesin-3	1	15	0.48	0.72	0.19		3	
Q9UIA0	Cytohesin-4	3	4	-0.02	-0.36	-0.32			
O60759	Cytohesin-interacting protein	2	19	0.12	-0.32	-0.41			5
P31785	Cytokine receptor common subunit gamma	1	5	-0.36	0.03	0.42			
Q8IUI8	Cytokine receptor-like factor 3	11	75	-0.03	-0.47	-0.48		5	
P21399	Cytoplasmic aconitase hydratase	8	35	-0.02	-0.23	-0.34			
Q14204	Cytoplasmic dynein 1 heavy chain 1	85	306	0.12	0.29	0.06			
Q13409	Cytoplasmic dynein 1 intermediate chain 2	9	50	0.00	-0.01	0.10			
Q9Y6G9	Cytoplasmic dynein 1 light intermediate chain 1	8	27	-0.10	-0.09	0.05			
O43237	Cytoplasmic dynein 1 light intermediate chain 2	5	18	0.18	-0.12	-0.13			
Q7L576	Cytoplasmic FMR1-interacting protein 1	2	49	-0.39	0.04	0.39			
Q96F07	Cytoplasmic FMR1-interacting protein 2	8	62	-0.02	0.30	0.28			
Q9UKF7	Cytoplasmic phosphatidylinositol transfer protein 1	2	10	-0.35	0.00	0.25			
P16333	Cytoplasmic protein NCK1	5	17	-0.28	-0.01	0.36			
O43639	Cytoplasmic protein NCK2	2	9	-0.10	-0.25	-0.14			

Q7Z7A3	Cytoplasmic tRNA 2-thiolation protein 1	3	3	-0.17	-0.19	-0.03			
Q2VPK5	Cytoplasmic tRNA 2-thiolation protein 2	1	1	-0.15	-0.14	0.01			
Q07065	Cytoskeleton-associated protein 4	7	20	0.52	0.18	-0.45			
Q14008	Cytoskeleton-associated protein 5	22	65	-0.05	-0.04	0.07			
P28838	Cytosol aminopeptidase	21	162	-0.24	0.21	0.47			
Q9H0P0	Cytosolic 5'-nucleotidase 3A	1	1	-0.26	0.11	0.37			
O00154	Cytosolic acyl coenzyme A thioester hydrolase	3	5	-0.95	-0.32	0.63	3		
Q9UPW5	Cytosolic carboxypeptidase 1	3	7	-0.17	0.25	0.53			
Q8NFI3	Cytosolic endo-beta-N-acetylglucosaminidase	6	18	-0.19	-0.46	-0.44		4	
Q9H6Q4	Cytosolic Fe-S cluster assembly factor NARFL	2	2	0.10	0.07	-0.04			
P53384	Cytosolic Fe-S cluster assembly factor NUBP1	5	11	0.02	-0.12	-0.09			
Q9Y5Y2	Cytosolic Fe-S cluster assembly factor NUBP2	6	30	-0.15	0.04	0.06			
Q96KP4	Cytosolic non-specific dipeptidase	24	238	0.03	0.17	0.09			
P49902	Cytosolic purine 5'-nucleotidase	1	6	0.04	-0.09	-0.02			
Q69YQ0	Cytospin-A	2	3	-0.52	-0.14	0.39			
Q5M775	Cytospin-B	5	10	-0.80	0.18	1.24	3		5
O43175	D-3-phosphoglycerate dehydrogenase	10	37	-0.09	-1.19	-1.66		5	5
Q96EP5	DAZ-associated protein 1	6	28	-0.30	0.05	0.21			
Q15038	DAZ-associated protein 2	1	1	0.04	-0.16	-0.20			
Q02338	D-beta-hydroxybutyrate dehydrogenase, mitochondrial	4	9	0.79	0.06	-0.64			3
Q5BKZ1	DBIRD complex subunit ZNF326	3	9	-0.76	-0.14	0.73	4		4
Q9UKG1	DCC-interacting protein 13-alpha	9	46	-0.03	0.21	0.27			
Q96GG9	DCN1-like protein 1	3	3	-0.51	-0.11	0.39			
Q8IWE4	DCN1-like protein 3	1	1	0.56	0.68	0.13			
Q9H773	dCTP pyrophosphatase 1	3	14	0.35	-0.32	-0.85			3
Q8TEB1	DDB1- and CUL4-associated factor 11	2	4	-0.53	-0.70	-0.17			
Q9NV06	DDB1- and CUL4-associated factor 13	4	7	0.18	-0.08	-0.24			
Q96JK2	DDB1- and CUL4-associated factor 5	1	2	-0.25	0.23	0.48			
P61962	DDB1- and CUL4-associated factor 7	5	22	-0.25	0.12	0.31			
Q5TAQ9	DDB1- and CUL4-associated factor 8	1	1	-0.18	0.13	0.31			
P30046	D-dopachrome decarboxylase	2	16	0.07	-0.02	-0.15			
Q96HY6	DDRKG domain-containing protein 1	6	34	0.25	0.04	-0.15			
Q9UER7	Death domain-associated protein 6	5	6	-0.10	-0.19	0.07			
Q9BTC0	Death-inducer obliterator 1	23	49	-0.09	-0.10	0.00			
Q96BY6	Dedicator of cytokinesis protein 10	31	86	-0.10	-0.28	-0.18			
Q5JSL3	Dedicator of cytokinesis protein 11	22	62	-0.08	-0.08	-0.02			
Q92608	Dedicator of cytokinesis protein 2	29	107	0.17	0.23	0.00			
Q8NF50	Dedicator of cytokinesis protein 8	30	105	0.00	-0.04	0.03			
Q9BZ29	Dedicator of cytokinesis protein 9	4	7	0.55	0.19	-0.35			
Q9BTZ2	Dehydrogenase/reductase SDR family member 4	7	47	0.02	-0.06	-0.09			
Q9Y394	Dehydrogenase/reductase SDR family member 7	6	29	0.16	0.73	0.48		5	4
Q8N5I4	Dehydrogenase/reductase SDR family member on chromosome X	1	1	0.02	0.27	0.25			
Q13011	Delta(3,5)-Delta(2,4)-dienoyl-CoA isomerase, mitochondrial	17	173	-0.01	0.06	0.13			
P30038	Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial	3	5	-0.41	0.07	0.49			
P54886	Delta-1-pyrroline-5-carboxylate synthase	12	33	0.25	0.04	-0.33			
P13716	Delta-aminolevulinic acid dehydratase	8	33	-0.06	-0.41	-0.29		4	
Q08495	Dematin	3	7	-0.14	-0.23	0.01			
Q8TEH3	DENN domain-containing protein 1A	2	4	-0.66	0.04	0.70			
Q8IV53	DENN domain-containing protein 1C	6	14	-0.08	0.08	0.14			
Q9H6A0	DENN domain-containing protein 2D	6	14	-0.11	-0.32	-0.35			
O75064	DENN domain-containing protein 4B	4	7	0.19	0.28	0.32			
Q5VZ89	DENN domain-containing protein 4C	9	16	0.20	0.41	0.20			
O43583	Density-regulated protein	6	29	0.01	-0.07	-0.14			
P27707	Deoxycytidine kinase	8	45	-0.17	-0.10	-0.06			
P32321	Deoxycytidylate deaminase	2	3	0.00	0.16	0.10			
Q9BU89	Deoxyhypusine hydroxylase	1	1	-0.10	-0.07	0.05			
P49366	Deoxyhypusine synthase	1	5	-0.01	-0.09	-0.11			
Q9Y3Z3	Deoxynucleoside triphosphate triphosphohydrolase SAMHD1	36	372	-0.20	-0.08	0.10			
Q9H147	Deoxynucleotidyltransferase terminal-interacting protein 1	6	12	0.16	0.11	0.06			
Q5QJE6	Deoxynucleotidyltransferase terminal-interacting protein 2	12	50	0.24	0.02	-0.16			
O00115	Deoxyribonuclease-2-alpha	1	13	-1.42	0.39	1.93	5		5
P33316	Deoxyuridine 5'-triphosphate nucleotidohydrolase, mitochondrial	9	38	-0.07	-0.24	-0.16			
O75140	DEP domain-containing protein 5	2	2	0.09	-0.15	-0.24			
Q9GZP9	Derlin-2	1	1	0.17	0.23	0.04			
P81605	Dermcidin	6	75	0.23	-0.24	-0.42			
Q6E0U4	Desmoglein-1	2	5	0.04	0.34	0.30			
P17661	Desmin	1	180	1.18	0.49	-0.68			
Q08554	Desmocollin-1	3	5	0.02	-1.54	-1.46			
Q14574	Desmocollin-3	1	1	0.18	-1.72	-1.92			
Q02413	Desmoglein-1	7	22	-0.04	0.58	-0.06		3	
P15924	Desmoplakin	7	12	0.79	0.86	0.08			
P60981	Destrin	7	93	-0.31	0.08	0.37			
Q9BW61	DET1- and DDB1-associated protein 1	3	6	0.02	0.13	0.10			
Q96JH7	Deubiquitinating protein VCIP135	20	50	-0.18	0.13	0.32			
Q9Y295	Developmentally-regulated GTP-binding protein 1	12	59	0.35	-0.09	-0.42			
P55039	Developmentally-regulated GTP-binding protein 2	5	15	0.20	0.01	-0.12			
Q9NR28	Diablo homolog, mitochondrial	7	34	-0.03	0.21	0.15			
P23743	Diacylglycerol kinase alpha	23	126	0.54	-0.86	-1.45	4	5	5
Q86XP1	Diacylglycerol kinase eta	1	2	-0.20	-0.17	0.03			
P52824	Diacylglycerol kinase theta	4	8	-0.90	0.12	0.96	5		5
Q13574	Diacylglycerol kinase zeta	7	25	-0.12	-0.41	-0.18			
Q9H4E7	Differentially expressed in FDCP 6 homolog	15	154	-0.15	0.04	0.16			
Q68CQ4	Digestive organ expansion factor homolog	1	1	0.73	-0.08	-0.83			
P09622	Dihydropolyl dehydrogenase, mitochondrial	15	132	0.26	0.09	-0.13			
P10515	Dihydropolyllysine-residue acetyltransferase component of pyruvate dehyd	12	73	0.52	0.07	-0.40			
P36957	Dihydropolyllysine-residue succinyltransferase component of 2-oxoglutarat	13	137	0.42	0.03	-0.18			

Q02127	Dihydroorotate dehydrogenase (quinone), mitochondrial	4	5	0.54	-0.16	-0.53			
P09417	Dihydropteridine reductase	6	39	0.55	-0.08	-0.70	5		5
Q16555	Dihydropyrimidinase-related protein 2	18	137	-0.74	0.05	0.62	4		4
O14531	Dihydropyrimidinase-related protein 4	1	1	-1.36	-0.27	1.09			
Q9BP06	Dihydropyrimidinase-related protein 5	1	20	-0.75	0.11	0.49			
Q12882	Dihydropyrimidine dehydrogenase	16	55	0.28	0.04	-0.21			
Q01459	Di-N-acetylchitinase	4	9	-0.16	0.41	0.72		4	3
P53634	Dipeptidyl peptidase 1	6	60	-1.33	0.41	1.60	5		5
Q9UHL4	Dipeptidyl peptidase 2	8	61	0.22	0.33	0.06		5	
Q9NY33	Dipeptidyl peptidase 3	15	64	-0.37	0.12	0.48			
P27487	Dipeptidyl peptidase 4	10	49	2.61	2.39	-0.25	5	5	
Q86T12	Dipeptidyl peptidase 9	4	9	-0.33	0.41	0.52			
Q95989	Diphosphoinositol polyphosphate phosphohydrolase 1	2	10	0.03	0.07	-0.18			
Q9NZJ9	Diphosphoinositol polyphosphate phosphohydrolase 2	3	13	-0.05	-0.33	-0.21			
P53602	Diphosphomevalonate decarboxylase	7	33	-0.67	0.04	0.74	4		3
Q9BQC3	Diphthamide biosynthesis protein 2	2	3	0.15	0.20	0.05			
Q8IYB7	DIS3-like exonuclease 2	3	4	-0.06	-0.02	-0.13			
Q14689	Disco-interacting protein 2 homolog A	1	1	-0.14	-0.07	0.08			
Q9P265	Disco-interacting protein 2 homolog B	1	2	-0.19	0.06	0.25			
O14672	Disintegrin and metalloproteinase domain-containing protein 10	5	16	0.02	0.71	0.82		5	5
P78536	Disintegrin and metalloproteinase domain-containing protein 17	1	1	0.17	0.35	0.19			
Q12959	Disks large homolog 1	3	8	0.26	0.18	-0.23			
Q92796	Disks large homolog 3	2	3	-0.14	-0.07	0.34			
Q9Y2H0	Disks large-associated protein 4	8	10	-0.17	-0.04	0.12			
P26358	DNA (cytosine-5)-methyltransferase 1	12	28	-0.07	0.08	0.09			
Q9Y6K1	DNA (cytosine-5)-methyltransferase 3A	2	8	-0.01	-0.19	0.06			
Q16531	DNA damage-binding protein 1	24	63	0.01	0.19	0.06			
Q92466	DNA damage-binding protein 2	3	7	0.07	-0.03	-0.07			
Q9NRW3	DNA dC->dU-editing enzyme APOBEC-3C	1	1	-0.10	0.39	0.49			
Q8IUX4	DNA dC->dU-editing enzyme APOBEC-3F	1	1	-0.14	0.02	0.14			
Q9HC16	DNA dC->dU-editing enzyme APOBEC-3G	2	14	-1.15	0.64	1.42	5	4	5
Q03468	DNA excision repair protein ERCC-6	2	3	-0.69	-0.18	0.52			
O00273	DNA fragmentation factor subunit alpha	9	52	0.07	-0.01	-0.20			
Q9ULG1	DNA helicase INO80	3	3	-0.15	0.06	0.21			
P49916	DNA ligase 3	12	44	-0.17	0.04	0.14			
Q9NPF5	DNA methyltransferase 1-associated protein 1	7	17	-0.19	-0.14	-0.03			
P40692	DNA mismatch repair protein Mlh1	1	1	0.03	0.03	-0.01			
P43246	DNA mismatch repair protein Msh2	12	19	0.00	-0.19	-0.11			
P52701	DNA mismatch repair protein Msh6	9	23	-0.14	-0.22	-0.07			
P06746	DNA polymerase beta	6	15	-0.51	-0.52	-0.03			
P28340	DNA polymerase delta catalytic subunit	1	3	0.10	-0.09	-0.19			
P49005	DNA polymerase delta subunit 2	1	2	-0.26	-0.41	-0.17			
Q15054	DNA polymerase delta subunit 3	2	2	-0.21	-0.13	0.09			
Q9NRF9	DNA polymerase epsilon subunit 3	3	5	-0.48	-0.31	0.32			
Q9NR33	DNA polymerase epsilon subunit 4	1	1	0.40	-0.05	-0.45			
P54098	DNA polymerase subunit gamma-1	2	3	0.58	0.30	-0.27			
Q9UHN1	DNA polymerase subunit gamma-2, mitochondrial	1	1	NA	NA	NA			
Q92889	DNA repair endonuclease XPF	2	4	0.11	-0.43	-0.11			
P23025	DNA repair protein complementing XP-A cells	1	9	-0.05	-0.05	0.03			
Q01831	DNA repair protein complementing XP-C cells	7	30	0.09	-0.23	-0.38			
P28715	DNA repair protein complementing XP-G cells	3	5	0.06	-0.25	-0.18			
Q92878	DNA repair protein RAD50	25	64	-0.19	-0.09	0.11			
P18887	DNA repair protein XRCC1	10	41	-0.25	-0.04	0.28			
Q13426	DNA repair protein XRCC4	2	4	-0.65	-0.33	0.31			
P49736	DNA replication licensing factor MCM2	6	9	-0.77	-0.42	0.27			
P25205	DNA replication licensing factor MCM3	6	8	-0.95	-0.65	0.37	4		5
P33991	DNA replication licensing factor MCM4	2	7	-0.90	-0.54	0.53	3		
P33992	DNA replication licensing factor MCM5	4	5	-1.38	-0.87	0.50	3		3
Q14566	DNA replication licensing factor MCM6	3	6	-0.96	-0.29	0.61	3		
P33993	DNA replication licensing factor MCM7	5	8	-1.34	-0.75	0.49	4		4
P11387	DNA topoisomerase 1	17	56	0.15	-0.21	-0.15			
Q02880	DNA topoisomerase 2-beta	34	107	-0.12	-0.08	0.19			
Q95985	DNA topoisomerase 3-beta-1	1	1	-0.21	0.10	0.32			
P27695	DNA-(apurinic or apyrimidinic site) lyase	13	128	0.31	-0.54	-0.84		4	5
Q60870	DNA/RNA-binding protein KIN17	5	7	-0.09	-0.15	-0.06			
P29372	DNA-3-methyladenine glycosylase	7	19	-0.36	-0.13	0.25			
Q13422	DNA-binding protein Ikaros	9	53	-0.22	-0.22	-0.03			
P48382	DNA-binding protein RFX5	10	24	-0.22	-0.05	0.08			
Q01826	DNA-binding protein SATB1	9	34	0.38	0.05	-0.29			
P38935	DNA-binding protein SMUBP-2	3	8	0.05	0.15	0.10			
P78527	DNA-dependent protein kinase catalytic subunit	69	312	-0.02	-0.06	-0.06			
Q96LW4	DNA-directed primase/polymerase protein	1	2	NA	NA	NA			
Q95602	DNA-directed RNA polymerase I subunit RPA1	9	21	0.15	-0.15	-0.29			
Q9H9Y6	DNA-directed RNA polymerase I subunit RPA2	3	4	0.44	0.20	-0.23			
O15446	DNA-directed RNA polymerase I subunit RPA34	5	11	0.04	-0.21	-0.22			
Q38726	DNA-directed RNA polymerase I subunit RPA43	1	1	0.24	-0.18	-0.42			
POCAP2	DNA-directed RNA polymerase II subunit GRINL1A	5	14	-0.02	0.02	-0.07			
Q6EEV4	DNA-directed RNA polymerase II subunit GRINL1A, isoforms 4/5	2	11	-0.02	-0.34	-0.31			
P24928	DNA-directed RNA polymerase II subunit RPB1	26	89	-0.05	-0.09	-0.11			
P30876	DNA-directed RNA polymerase II subunit RPB2	22	103	0.15	-0.05	-0.10			
P19387	DNA-directed RNA polymerase II subunit RPB3	5	29	0.07	-0.05	-0.20			
O15514	DNA-directed RNA polymerase II subunit RPB4	2	10	-0.23	-0.41	0.11			
P62487	DNA-directed RNA polymerase II subunit RPB7	2	5	-0.06	-0.15	-0.05			
P36954	DNA-directed RNA polymerase II subunit RPB9	2	2	-0.01	0.01	0.03			
Q9Y2Y1	DNA-directed RNA polymerase III subunit RPC10	1	2	-0.43	-0.12	0.32			
Q9NW08	DNA-directed RNA polymerase III subunit RPC2	1	3	0.02	-0.13	-0.39			

Q9BU14	DNA-directed RNA polymerase III subunit RPC3	2	4	-0.21	-0.07	-0.05			
Q9NVU0	DNA-directed RNA polymerase III subunit RPC5	1	1	0.07	-0.59	-0.68			
Q9H1D9	DNA-directed RNA polymerase III subunit RPC6	1	2	0.10	0.10	0.01			
Q9BT43	DNA-directed RNA polymerase III subunit RPC7-like	1	4	-0.12	-0.35	-0.20			
O00411	DNA-directed RNA polymerase, mitochondrial	1	1	-0.96	-0.74	0.24			
O15160	DNA-directed RNA polymerases I and III subunit RPAC1	5	19	-0.07	-0.18	-0.19			
Q9Y2S0	DNA-directed RNA polymerases I and III subunit RPAC2	3	18	0.20	-0.09	0.01			
P19388	DNA-directed RNA polymerases I, II, and III subunit RPABC1	6	23	-0.04	-0.16	-0.18			
P61218	DNA-directed RNA polymerases I, II, and III subunit RPABC2	2	12	-0.08	-0.29	-0.19			
P52434	DNA-directed RNA polymerases I, II, and III subunit RPABC3	4	25	0.07	-0.27	-0.23			
P53803	DNA-directed RNA polymerases I, II, and III subunit RPABC4	1	1	0.05	-0.08	-0.12			
P62875	DNA-directed RNA polymerases I, II, and III subunit RPABC5	2	4	0.06	-0.02	-0.15			
P31689	DnaJ homolog subfamily A member 1	7	41	-0.04	-0.10	-0.04			
O60884	DnaJ homolog subfamily A member 2	9	12	-0.07	-0.36	-0.26			
Q96EY1	DnaJ homolog subfamily A member 3, mitochondrial	5	20	0.37	-0.16	-0.55			
P25685	DnaJ homolog subfamily B member 1	15	66	0.20	-0.23	-0.58			
Q9UBS4	DnaJ homolog subfamily B member 11	6	23	-0.45	0.17	0.74			5
P25686	DnaJ homolog subfamily B member 2	4	19	0.63	0.15	0.17	3		
O75190	DnaJ homolog subfamily B member 6	4	14	0.14	0.30	0.23			
Q96KC8	DnaJ homolog subfamily C member 1	1	1	0.10	0.71	0.62			
Q8IXB1	DnaJ homolog subfamily C member 10	3	4	-0.14	0.04	0.18			
Q9NVH1	DnaJ homolog subfamily C member 11	5	12	0.07	-0.04	-0.17			
O75165	DnaJ homolog subfamily C member 13	11	26	-0.12	0.01	-0.02			
Q9NVM6	DnaJ homolog subfamily C member 17	6	13	-0.66	-0.15	0.26			
Q99543	DnaJ homolog subfamily C member 2	8	17	0.14	-0.13	-0.20			
Q5F1R6	DnaJ homolog subfamily C member 21	2	2	0.20	-0.16	-0.36			
Q13217	DnaJ homolog subfamily C member 3	1	4	-0.12	0.50	0.62			
Q99615	DnaJ homolog subfamily C member 7	10	36	-0.24	0.03	0.37			
O75937	DnaJ homolog subfamily C member 8	14	84	-0.20	-0.19	0.00			
Q8WXX5	DnaJ homolog subfamily C member 9	12	50	0.14	-0.21	-0.17			
Q5SXM8	DNL-type zinc finger protein	1	8	0.12	0.06	-0.26			
Q99704	Docking protein 1	4	7	-0.29	-0.01	0.28			
O60496	Docking protein 2	10	76	-0.95	0.44	1.43	5		5
Q7L591	Docking protein 3	1	1	NA	NA	NA			
O60762	Dolichol-phosphate mannosyltransferase	4	6	-0.17	0.12	0.22			
Q9P2X0	Dolichol-phosphate mannosyltransferase subunit 3	1	6	0.49	0.91	0.41			
P39656	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase 48 kDa subunit 1	8	46	0.41	0.49	-0.01			5
P04843	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 1	27	142	0.27	0.34	-0.01			
P04844	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit 2	7	29	0.38	0.32	0.03			
P46977	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit STT1	3	16	0.66	0.68	0.20	4		4
Q8TCJ2	Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit STT2	2	3	0.43	0.21	-0.14			
Q9Y673	Dolichyl-phosphate beta-glucosyltransferase	3	7	0.12	0.31	0.19			
P49959	Double-strand break repair protein MRE11A	14	47	-0.35	-0.15	0.19			
O60216	Double-strand-break repair protein rad21 homolog	19	103	-0.15	-0.17	-0.01			
O95793	Double-stranded RNA-binding protein Staufien homolog 1	5	8	-0.20	0.00	0.20			
Q9NUL3	Double-stranded RNA-binding protein Staufien homolog 2	5	11	-0.32	-0.06	0.32			
P55265	Double-stranded RNA-specific adenosine deaminase	37	170	-0.01	-0.14	-0.03			
P78563	Double-stranded RNA-specific editase 1	1	2	0.36	0.09	-0.27			
Q9NS39	Double-stranded RNA-specific editase B2	1	1	NA	NA	NA			
O14972	Down syndrome critical region protein 3	1	1	-0.26	0.03	0.29			
Q14919	Dr1-associated corepressor	5	36	-0.52	-0.31	0.06			
Q16643	Drebrin	10	41	1.15	0.51	-0.61	5	4	3
Q9UJU6	Drebrin-like protein	25	275	-0.22	0.22	0.36			
Q8TEA8	D-tyrosyl-tRNA(Tyr) deacylase 1	2	13	0.02	0.21	0.25			
Q02750	Dual specificity mitogen-activated protein kinase kinase 1	7	40	0.10	-0.09	-0.15			
P36507	Dual specificity mitogen-activated protein kinase kinase 2	6	28	-0.30	0.08	0.35			
P46734	Dual specificity mitogen-activated protein kinase kinase 3	6	22	-0.04	0.39	0.24			
P45985	Dual specificity mitogen-activated protein kinase kinase 4	4	15	-0.17	-0.03	0.17			
P52564	Dual specificity mitogen-activated protein kinase kinase 6	4	23	0.19	0.16	-0.05			
P49759	Dual specificity protein kinase CLK1	2	3	0.25	0.17	-0.09			
P28562	Dual specificity protein phosphatase 1	1	1	-0.24	0.09	0.34			
Q9UNI6	Dual specificity protein phosphatase 12	2	6	-0.16	0.31	0.48			
Q9BVJ7	Dual specificity protein phosphatase 23	5	17	-0.66	-0.15	0.60	5		3
P51452	Dual specificity protein phosphatase 3	5	11	0.00	0.01	0.14			
Q13627	Dual specificity tyrosine-phosphorylation-regulated kinase 1A	2	2	-0.25	-0.14	0.11			
Q14203	Dynactin subunit 1	26	126	0.12	-0.02	-0.04			
Q13561	Dynactin subunit 2	20	109	-0.14	-0.05	-0.05			
O75935	Dynactin subunit 3	6	18	0.26	0.08	-0.13			
Q9UJW0	Dynactin subunit 4	6	17	0.07	-0.03	-0.09			
Q9BTE1	Dynactin subunit 5	1	3	-0.45	-0.08	0.00			
O00399	Dynactin subunit 6	3	8	-0.22	-0.32	-0.10			
O00429	Dynamin-1-like protein	10	37	-0.03	-0.04	0.01			
P50570	Dynamin-2	27	165	-0.20	0.14	0.39			
O60313	Dynamin-like 120 kDa protein, mitochondrial	28	93	0.05	-0.15	-0.16			
Q9C0G6	Dynein heavy chain 6, axonemal	1	10	0.07	0.07	-0.25			
Q96JB1	Dynein heavy chain 8, axonemal	2	3	0.11	-0.27	-0.38			
P63167	Dynein light chain 1, cytoplasmic	2	26	-0.44	0.16	0.28			
Q96FJ2	Dynein light chain 2, cytoplasmic	4	61	0.24	0.16	-0.01			
Q9NP97	Dynein light chain roadblock-type 1	3	18	0.08	-0.03	0.05			
P51808	Dynein light chain Tctex-type 3	1	3	-0.04	0.08	0.26			
Q96EV8	Dysbindin	3	15	-0.33	-0.21	0.13			
Q96L91	E1A-binding protein p400	18	51	-0.18	-0.06	0.05			
Q9UII4	E3 ISG15--protein ligase HERC5	1	1	-0.20	-0.02	0.18			
O00257	E3 SUMO-protein ligase CBX4	3	3	0.16	0.02	-0.14			
Q96MF7	E3 SUMO-protein ligase NSE2	1	1	-0.52	-0.59	-0.07			
O75925	E3 SUMO-protein ligase PIAS1	2	4	-0.03	0.09	0.13			

Q8N2W9	E3 SUMO-protein ligase PIAS4	1	1	-0.27	-0.12	0.15			
P49792	E3 SUMO-protein ligase RanBP2	50	182	-0.08	0.07	0.08			
Q14258	E3 ubiquitin/ISG15 ligase TRIM25	11	52	-0.07	0.14	0.17			
Q9UKV5	E3 ubiquitin-protein ligase AMFR	2	2	0.47	0.44	-0.01			
Q9Y4X5	E3 ubiquitin-protein ligase ARIH1	1	8	0.09	0.18	0.09			
O95376	E3 ubiquitin-protein ligase ARIH2	2	4	0.03	0.00	-0.03			
Q5VTR2	E3 ubiquitin-protein ligase BRE1A	12	29	-0.23	-0.20	0.13			
O75150	E3 ubiquitin-protein ligase BRE1B	9	25	-0.31	-0.09	0.25			
P22681	E3 ubiquitin-protein ligase CBL	6	10	-0.07	-0.11	-0.17			
Q13191	E3 ubiquitin-protein ligase CBL-B	4	6	-0.65	0.23	0.85			
Q96EP1	E3 ubiquitin-protein ligase CHFR	1	1	-0.21	0.35	0.57			
Q9UNE7	E3 ubiquitin-protein ligase CHIP	2	5	0.07	-0.17	-0.16			
Q8TDB6	E3 ubiquitin-protein ligase DTX3L	10	22	0.22	0.17	0.18			
Q75N03	E3 ubiquitin-protein ligase Hakai	2	6	-0.05	0.06	-0.12			
Q9ULT8	E3 ubiquitin-protein ligase HECTD1	6	10	-0.19	-0.04	0.11			
Q5T447	E3 ubiquitin-protein ligase HECTD3	5	25	-0.09	0.23	0.24			
Q7Z6Z7	E3 ubiquitin-protein ligase HUWE1	30	134	0.14	0.13	0.00			
Q96J02	E3 ubiquitin-protein ligase Itchy homolog	3	8	0.25	0.58	0.38			
Q9P0J7	E3 ubiquitin-protein ligase KCMF1	1	1	-0.14	0.04	0.18			
Q6UWE0	E3 ubiquitin-protein ligase LRSAM1	3	7	0.58	0.70	-0.10			
Q86YT6	E3 ubiquitin-protein ligase MIB1	1	1	-0.30	0.02	0.30			
Q9HCL7	E3 ubiquitin-protein ligase MSL2	4	4	-0.12	-0.01	0.16			
O43164	E3 ubiquitin-protein ligase Praja-2	1	1	-0.95	-0.77	0.19			
Q7Z6E9	E3 ubiquitin-protein ligase RBBP6	10	24	-0.41	-0.11	0.16			
Q06587	E3 ubiquitin-protein ligase RING1	4	13	-0.06	-0.04	0.09			
Q99496	E3 ubiquitin-protein ligase RING2	2	11	0.08	0.02	-0.01			
Q9BV68	E3 ubiquitin-protein ligase RNF126	2	4	-0.03	0.05	0.37			
O43567	E3 ubiquitin-protein ligase RNF13	2	8	-0.52	0.60	1.13			3
Q86XS8	E3 ubiquitin-protein ligase RNF130	1	9	0.38	0.79	0.43			
Q9H6Y7	E3 ubiquitin-protein ligase RNF167	1	1	-3.68	-2.16	1.54			
Q8NCN4	E3 ubiquitin-protein ligase RNF169	5	8	-0.67	0.01	0.68			
Q9P0P0	E3 ubiquitin-protein ligase RNF181	1	1	NA	NA	NA			
Q63HN8	E3 ubiquitin-protein ligase RNF213	65	246	0.05	0.22	0.21			
Q9NWF9	E3 ubiquitin-protein ligase RNF216	1	1	-0.58	0.06	0.62			
Q96BH1	E3 ubiquitin-protein ligase RNF25	1	1	-0.74	-0.61	0.14			
Q96EP0	E3 ubiquitin-protein ligase RNF31	8	27	0.14	0.20	0.16			
Q969K3	E3 ubiquitin-protein ligase RNF34	1	1	0.59	0.45	-0.13			
P19474	E3 ubiquitin-protein ligase TRIM21	4	18	0.00	0.24	0.24			
Q8IYM9	E3 ubiquitin-protein ligase TRIM22	4	9	-0.30	0.04	0.24			
Q13049	E3 ubiquitin-protein ligase TRIM32	3	5	0.06	0.03	-0.04			
Q9UPN9	E3 ubiquitin-protein ligase TRIM33	5	8	-0.46	-0.11	0.35			
Q8WW44	E3 ubiquitin-protein ligase TRIM41	2	5	-0.16	-0.29	-0.15			
Q9BRZ2	E3 ubiquitin-protein ligase TRIM56	7	23	-0.17	0.01	0.16			
Q14669	E3 ubiquitin-protein ligase TRIP12	15	70	-0.38	-0.06	0.42			
Q8IWW7	E3 ubiquitin-protein ligase UBR1	5	9	0.03	0.22	0.18			
Q8IWW8	E3 ubiquitin-protein ligase UBR2	1	1	-0.08	0.69	0.77			
Q5T4S7	E3 ubiquitin-protein ligase UBR4	26	58	-0.05	0.06	-0.07			
O95071	E3 ubiquitin-protein ligase UBR5	5	7	0.09	-0.07	-0.19			
Q96PU4	E3 ubiquitin-protein ligase UHRF2	3	4	0.75	0.29	-0.52			
P98170	E3 ubiquitin-protein ligase XIAP	4	15	-0.14	0.00	0.16			
Q96JP5	E3 ubiquitin-protein ligase ZFP91	4	26	-0.41	0.01	0.24			
Q8NHG8	E3 ubiquitin-protein ligase ZNRF2	1	1	0.02	0.68	0.64			
O94874	E3 UFM1-protein ligase 1	12	48	0.31	0.12	-0.31			
Q07108	Early activation antigen CD69	1	2	0.58	1.64	1.06			
Q15075	Early endosome antigen 1	27	72	-0.18	0.00	0.20			
O95834	Echinoderm microtubule-associated protein-like 2	12	54	0.13	0.28	0.14			
Q32P44	Echinoderm microtubule-associated protein-like 3	18	106	-0.01	-0.01	-0.03			
Q9HC35	Echinoderm microtubule-associated protein-like 4	22	94	0.97	0.68	-0.43	5	5	
Q6ZMW3	Echinoderm microtubule-associated protein-like 6	1	2	-0.88	-1.39	-0.50			
Q9BSW2	EF-hand calcium-binding domain-containing protein 4B	3	5	-0.45	0.00	0.45			
Q96C19	EF-hand domain-containing protein D2	21	404	-1.26	0.67	1.62	5	5	5
O43854	EGF-like repeat and discoidin I-like domain-containing protein 3	1	1	-0.03	-0.56	-0.52			
Q9GZT9	Egl nine homolog 1	2	15	0.00	0.10	0.08			
Q8N3D4	EH domain-binding protein 1-like protein 1	9	22	-0.13	0.02	0.21			
Q9H4M9	EH domain-containing protein 1	18	283	0.12	0.59	0.35		5	
Q9NZN3	EH domain-containing protein 3	1	58	-0.25	-0.09	0.16			
Q9H223	EH domain-containing protein 4	7	25	-0.01	0.40	0.42			
Q14657	EKC/KEOPS complex subunit LAGE3	5	20	-0.01	-0.15	0.01			
Q9Y3C4	EKC/KEOPS complex subunit TPRKB	2	12	0.15	-0.27	-0.25			
Q15717	ELAV-like protein 1	13	93	-0.26	-0.27	0.11			
P13804	Electron transfer flavoprotein subunit alpha, mitochondrial	14	142	0.35	-0.16	-0.47			5
P38117	Electron transfer flavoprotein subunit beta	18	216	0.30	-0.21	-0.55			
Q16134	Electron transfer flavoprotein-ubiquinone oxidoreductase, mitochondrial	7	16	0.03	0.15	0.11			
Q8IUD2	ELKS/Rab6-interacting/CAST family member 1	3	6	-0.02	-0.01	0.02			
Q6PJG2	ELM2 and SANT domain-containing protein 1	8	14	-0.14	-0.03	0.13			
Q8IZ81	ELMO domain-containing protein 2	1	1	0.09	0.03	-0.08			
P68104	Elongation factor 1-alpha 1	23	1732	0.15	0.17	-0.18			
P24534	Elongation factor 1-beta	10	70	0.21	-0.01	-0.10			
P29692	Elongation factor 1-delta	10	178	0.16	0.03	0.05			
P26641	Elongation factor 1-gamma	15	124	0.29	0.17	-0.28			
P13639	Elongation factor 2	40	568	0.24	0.06	-0.25			
Q96RP9	Elongation factor G, mitochondrial	11	27	0.43	0.14	-0.28			
P43897	Elongation factor Ts, mitochondrial	4	15	0.30	0.07	-0.10			
Q7Z2Z2	Elongation factor Tu GTP-binding domain-containing protein 1	7	13	0.19	0.14	0.01			
P49411	Elongation factor Tu, mitochondrial	27	379	0.46	0.19	-0.13			
O95163	Elongator complex protein 1	7	13	0.12	0.20	0.07			

Q6IA86	Elongator complex protein 2	1	1	-0.59	-0.30	0.29			
Q9H9T3	Elongator complex protein 3	2	9	0.03	0.10	0.07			
Q96EB1	Elongator complex protein 4	1	1	-0.25	-0.32	-0.07			
Q8TE02	Elongator complex protein 5	1	1	-0.19	-0.01	0.17			
Q0PNE2	Elongator complex protein 6	2	2	0.10	-0.21	-0.31			
Q6PCB8	Embigin	1	2	0.74	1.22	0.49			
Q96FZ2	Embryonic stem cell-specific 5-hydroxymethylcytosine-binding protein	1	1	NA	NA	NA			
P50402	Emerin	5	41	0.25	0.05	-0.24			
Q9Y6C2	EMILIN-1	1	1	NA	NA	NA			
Q9UI08	Ena/VASP-like protein	25	344	-0.44	-0.44	0.20			
Q969S2	Endonuclease 8-like 2	1	1	NA	NA	NA			
O94919	Endonuclease domain-containing 1 protein	2	5	-0.34	0.09	0.43			
Q14249	Endonuclease G, mitochondrial	2	5	-0.09	0.31	0.36			
P78549	Endonuclease III-like protein 1	3	4	-0.24	-0.11	0.04			
Q99961	Endophilin-A2	10	39	-0.29	0.19	0.56			4
Q9Y371	Endophilin-B1	10	52	-0.44	0.23	0.53			4
Q9NR46	Endophilin-B2	7	47	0.16	0.01	0.06			
Q9NZ08	Endoplasmic reticulum aminopeptidase 1	17	69	0.20	0.34	0.37			
Q6P179	Endoplasmic reticulum aminopeptidase 2	8	27	-0.30	-0.01	0.23			
Q96DZ1	Endoplasmic reticulum lectin 1	2	2	-0.14	0.31	0.45			
Q7Z2K6	Endoplasmic reticulum metalloproteinase 1	7	18	0.20	0.95	0.56		5	
P30040	Endoplasmic reticulum resident protein 29	8	107	0.08	0.05	0.01			
Q9BS26	Endoplasmic reticulum resident protein 44	5	11	-0.47	0.33	0.91			4
Q969X5	Endoplasmic reticulum-Golgi intermediate compartment protein 1	6	20	0.28	0.71	0.31		5	
P14625	Endoplasmic reticulum chaperone	36	304	0.21	0.47	0.28		5	
Q9UPY3	Endoribonuclease Dicer	1	1	0.28	0.32	0.04			
O60869	Endothelial differentiation-related factor 1	6	57	-0.08	-0.14	0.01			
Q92556	Engulfment and cell motility protein 1	15	63	-0.15	-0.03	-0.10			
Q96J33	Engulfment and cell motility protein 2	10	54	-0.02	0.27	0.27			
Q14511	Enhancer of filamentation 1	4	5	-0.59	0.35	0.93			
Q96F86	Enhancer of mRNA-decapping protein 3	5	15	0.01	-0.09	-0.21			
Q6P2E9	Enhancer of mRNA-decapping protein 4	20	91	0.08	0.00	-0.10			
Q52LR7	Enhancer of polycomb homolog 2	1	1	0.17	0.15	-0.02			
P84090	Enhancer of rudimentary homolog	3	19	0.04	0.04	-0.12			
Q9UHY7	Enolase-phosphatase E1	4	15	0.30	-0.19	-0.27			
P42126	Enoyl-CoA delta isomerase 1, mitochondrial	3	22	0.13	0.18	0.10			
O75521	Enoyl-CoA delta isomerase 2, mitochondrial	7	29	0.39	-0.10	-0.37			5
Q86YB7	Enoyl-CoA hydratase domain-containing protein 2, mitochondrial	1	9	0.15	-0.07	-0.27			
P30084	Enoyl-CoA hydratase, mitochondrial	15	147	0.22	-0.05	-0.23			
Q92817	Envoplakin	1	1	NA	NA	NA			
O95936	Eomesodermin homolog	5	7	-0.36	0.38	0.71			
Q8N611	EP300-interacting inhibitor of differentiation 2	1	1	0.22	-0.01	-0.23			
P42566	Epidermal growth factor receptor substrate 15	14	44	0.10	0.30	0.29			
Q9UBC2	Epidermal growth factor receptor substrate 15-like 1	14	37	-0.56	0.13	0.52	5		5
P61916	Epididymal secretory protein E1	6	21	-0.42	0.78	1.26		4	5
Q9Y2E5	Epididymis-specific alpha-mannosidase	2	2	-0.71	-0.16	0.56			
Q9NRG7	Epimerase family protein SDR39U1	2	3	-0.06	0.23	0.28			
P58107	Epiplakin	9	38	0.18	-0.76	-0.87			
Q96J88	Epithelial-stromal interaction protein 1	3	3	-0.22	0.21	0.44			
Q9Y6I3	Epsin-1	3	9	-0.24	0.08	0.52			
Q8N766	ER membrane protein complex subunit 1	5	11	0.07	0.29	0.37			
Q5UCC4	ER membrane protein complex subunit 10	2	2	0.13	0.35	0.23			
Q15006	ER membrane protein complex subunit 2	3	10	-0.28	0.01	0.29			
Q9P0I2	ER membrane protein complex subunit 3	1	2	0.10	0.47	0.37			
Q5J8M3	ER membrane protein complex subunit 4	1	1	-0.11	-0.07	0.04			
Q9NPA0	ER membrane protein complex subunit 7	1	1	0.05	-0.04	-0.09			
O43402	ER membrane protein complex subunit 8	1	3	NA	NA	NA			
O94905	Erlin-2	3	5	-0.20	-0.08	0.14			
Q96HE7	ERO1-like protein alpha	2	7	0.86	0.76	-0.21	4		3
P27105	Erythrocyte band 7 integral membrane protein	8	111	-0.77	0.60	1.25	4		5
P30042	ES1 protein homolog, mitochondrial	14	128	-0.07	-0.17	-0.22			
Q9H501	ESF1 homolog	3	4	0.04	-0.43	-0.12			
Q9H4I9	Essential MCU regulator, mitochondrial	1	2	0.09	0.27	0.19			
Q9H0W9	Ester hydrolase C11orf54	4	14	-0.10	-0.35	-0.32			
Q8NBQ5	Estradiol 17-beta-dehydrogenase 11	2	3	0.48	0.43	-0.04			
Q53GQ0	Estradiol 17-beta-dehydrogenase 12	4	18	0.16	0.12	-0.07			
Q92506	Estradiol 17-beta-dehydrogenase 8	8	50	0.19	-0.23	-0.39			
Q99447	Ethanolamine-phosphate cytidyltransferase	9	26	-0.47	0.07	0.42			
Q9NTX5	Ethylmalonyl-CoA decarboxylase	10	41	0.08	-0.22	-0.65			3
P19419	ETS domain-containing protein Elk-1	1	1	0.20	-0.56	-0.75			
P50548	ETS domain-containing transcription factor ERF	2	2	-0.53	-0.12	0.42			
P32519	ETS-related transcription factor Elf-1	9	55	-0.15	-0.07	0.09			
Q15723	ETS-related transcription factor Elf-2	6	11	-0.35	-0.06	0.26			
O00418	Eukaryotic elongation factor 2 kinase	1	1	NA	NA	NA			
P60842	Eukaryotic initiation factor 4A-I	9	275	0.36	0.36	0.12			
Q14240	Eukaryotic initiation factor 4A-II	3	203	0.44	0.08	-0.31			
P38919	Eukaryotic initiation factor 4A-III	16	135	0.08	-0.07	-0.12			
P15170	Eukaryotic peptide chain release factor GTP-binding subunit ERF3A	13	58	0.44	-0.08	-0.54			
P62495	Eukaryotic peptide chain release factor subunit 1	5	27	0.46	0.22	-0.25			
O43324	Eukaryotic translation elongation factor 1 epsilon-1	1	2	-0.05	-0.05	0.01			
P47813	Eukaryotic translation initiation factor 1A, X-chromosomal	7	32	0.43	-0.07	-0.62			3
O60739	Eukaryotic translation initiation factor 1b	3	11	-0.01	0.03	0.04			
P05198	Eukaryotic translation initiation factor 2 subunit 1	15	92	0.21	0.11	-0.11			
P20042	Eukaryotic translation initiation factor 2 subunit 2	12	31	0.22	0.27	-0.14			
P41091	Eukaryotic translation initiation factor 2 subunit 3	15	71	0.29	0.14	-0.07			
Q9BY44	Eukaryotic translation initiation factor 2A	12	29	0.13	0.09	-0.09			

Q9BQI3	Eukaryotic translation initiation factor 2-alpha kinase 1	1	1	0.32	0.00	-0.32			
P41214	Eukaryotic translation initiation factor 2D	5	10	0.26	-0.29	-0.59			
Q14152	Eukaryotic translation initiation factor 3 subunit A	36	182	0.37	0.29	-0.10			
P55884	Eukaryotic translation initiation factor 3 subunit B	18	94	0.41	0.28	-0.18			
Q99613	Eukaryotic translation initiation factor 3 subunit C	28	161	0.32	0.20	-0.26			
O15371	Eukaryotic translation initiation factor 3 subunit D	11	33	0.29	0.28	-0.13			
P60228	Eukaryotic translation initiation factor 3 subunit E	13	88	0.27	0.28	-0.12			
O00303	Eukaryotic translation initiation factor 3 subunit F	8	59	0.30	0.20	-0.20			
O75821	Eukaryotic translation initiation factor 3 subunit G	6	14	-0.78	-0.46	0.39			
O15372	Eukaryotic translation initiation factor 3 subunit H	12	65	0.37	0.19	-0.19			
Q13347	Eukaryotic translation initiation factor 3 subunit I	12	80	0.16	0.12	-0.12			
O75822	Eukaryotic translation initiation factor 3 subunit J	9	18	0.03	0.01	-0.04			
Q9UBQ5	Eukaryotic translation initiation factor 3 subunit K	6	22	0.55	0.23	-0.28			
Q9Y262	Eukaryotic translation initiation factor 3 subunit L	15	73	0.47	0.37	-0.08			
Q7L2H7	Eukaryotic translation initiation factor 3 subunit M	4	19	0.33	0.26	-0.07			
Q04637	Eukaryotic translation initiation factor 4 gamma 1	19	82	0.12	0.09	-0.05			
P78344	Eukaryotic translation initiation factor 4 gamma 2	10	26	0.14	0.07	0.16			
O43432	Eukaryotic translation initiation factor 4 gamma 3	3	11	-0.37	0.07	0.53			
P23588	Eukaryotic translation initiation factor 4B	12	78	0.14	0.01	-0.20			
P06730	Eukaryotic translation initiation factor 4E	5	32	-0.09	-0.32	-0.23			
Q9NRA8	Eukaryotic translation initiation factor 4E transporter	2	2	-0.61	-0.12	0.49			
Q8N5X7	Eukaryotic translation initiation factor 4E type 3	1	2	0.21	-0.04	-0.26			
Q13541	Eukaryotic translation initiation factor 4E-binding protein 1	2	7	0.01	-0.19	0.20			
Q13542	Eukaryotic translation initiation factor 4E-binding protein 2	2	13	-0.13	0.08	0.16			
Q15056	Eukaryotic translation initiation factor 4H	6	29	-0.18	-0.11	0.19			
P55010	Eukaryotic translation initiation factor 5	12	44	0.10	0.09	0.07			
P63241	Eukaryotic translation initiation factor 5A-1	8	187	0.19	-0.12	-0.19			
O60841	Eukaryotic translation initiation factor 5B	21	55	0.20	-0.02	-0.16			
P56537	Eukaryotic translation initiation factor 6	6	49	-0.11	0.00	0.01			
Q9NV70	Exocyst complex component 1	2	4	0.13	0.34	0.18			
Q96KP1	Exocyst complex component 2	6	8	-0.04	0.07	0.02			
O60645	Exocyst complex component 3	2	2	-0.09	0.11	0.20			
Q96A65	Exocyst complex component 4	5	15	0.18	0.26	0.17			
O00471	Exocyst complex component 5	1	1	-0.28	0.05	0.33			
Q8TAG9	Exocyst complex component 6	1	4	-0.18	0.10	0.28			
Q9Y2D4	Exocyst complex component 6B	3	4	0.07	0.03	0.04			
Q9UPT5	Exocyst complex component 7	1	1	-0.02	-0.08	-0.06			
Q8IYI6	Exocyst complex component 8	4	6	-0.52	-0.20	0.46			
Q9Y3B2	Exosome complex component CSL4	2	4	-0.03	0.09	0.09			
Q5RKV6	Exosome complex component MTR3	7	40	-0.05	-0.24	-0.20			
Q13868	Exosome complex component RRP4	7	28	0.08	-0.23	-0.25			
Q9NQY5	Exosome complex component RRP40	4	7	0.71	0.01	-0.42			
Q9NPD3	Exosome complex component RRP41	5	23	0.12	0.05	-0.06			
Q15024	Exosome complex component RRP42	3	6	0.11	-0.12	-0.34			
Q96B26	Exosome complex component RRP43	3	11	0.13	-0.16	-0.27			
Q06265	Exosome complex component RRP45	2	4	0.17	0.12	-0.05			
Q9NQY4	Exosome complex component RRP46	5	19	0.02	-0.30	-0.36			
Q9Y2L1	Exosome complex exonuclease RRP44	8	28	0.12	-0.03	-0.29			
Q01780	Exosome component 10	13	40	-0.08	-0.15	-0.08			
O14980	Exportin-1	10	26	0.15	0.18	-0.04			
P55060	Exportin-2	11	46	0.15	-0.17	-0.14			
Q9C0E2	Exportin-4	2	7	0.37	0.29	-0.08			
Q9HAV4	Exportin-5	4	13	0.21	0.07	-0.16			
Q9UIA9	Exportin-7	8	26	0.17	0.16	-0.04			
O43592	Exportin-T	1	2	0.49	0.19	-0.30			
Q9BSJ8	Extended synaptotagmin-1	25	186	0.24	-0.05	-0.18			
A0FGR8	Extended synaptotagmin-2	15	80	-0.31	-0.18	0.21			
P15311	Ezrin	25	577	0.55	0.29	-0.08			
Q9Y5B9	FACT complex subunit SPT16	24	70	0.19	0.08	-0.12			
Q08945	FACT complex subunit SSRP1	15	86	0.20	0.08	-0.07			
P52907	F-actin-capping protein subunit alpha-1	14	261	0.29	0.20	-0.01			
P47755	F-actin-capping protein subunit alpha-2	7	100	-0.14	-0.07	-0.05			
P47756	F-actin-capping protein subunit beta	16	188	0.09	0.17	0.01			
P23610	Factor VIII intron 22 protein	2	3	0.20	0.15	-0.03			
Q8NFF5	FAD synthase	1	1	NA	NA	NA			
Q96CU9	FAD-dependent oxidoreductase domain-containing protein 1	1	1	0.25	-0.27	-0.52			
P55789	FAD-linked sulfhydryl oxidase ALR	3	24	0.12	0.41	0.27		5	
Q96AE4	Far upstream element-binding protein 1	30	355	-0.10	-0.08	0.03			
Q92945	Far upstream element-binding protein 2	36	339	-0.25	-0.24	0.07			
Q96124	Far upstream element-binding protein 3	16	127	-0.22	-0.14	0.14			
P14324	Farnesyl pyrophosphate synthase	5	34	-0.22	0.12	0.31			
Q9UNN5	FAS-associated factor 1	4	10	-0.02	0.00	-0.07			
Q96CS3	FAS-associated factor 2	5	10	0.28	0.21	-0.32			
Q8TES7	Fas-binding factor 1	1	4	NA	NA	NA			
Q7L8L6	FAST kinase domain-containing protein 5	1	1	0.52	0.33	-0.20			
P49327	Fatty acid synthase	17	46	-0.32	0.04	0.38			
Q01469	Fatty acid-binding protein, epidermal	4	11	-0.01	-0.59	-0.20			
P51648	Fatty aldehyde dehydrogenase	1	2	-0.58	-0.19	0.39			
Q9UK22	F-box only protein 2	1	1	NA	NA	NA			
Q9NVF7	F-box only protein 28	2	7	-0.18	-0.35	-0.05			
Q9UK99	F-box only protein 3	4	5	-0.08	0.14	0.22			
Q6PIJ6	F-box only protein 38	2	3	0.97	0.28	-0.69			
Q9NRD1	F-box only protein 6	2	3	-0.47	0.41	0.65			
Q9Y3I1	F-box only protein 7	1	7	-0.20	0.08	0.31			
P0C2W1	F-box/SPRY domain-containing protein 1	1	2	0.40	0.35	-0.04			
Q9BZK7	F-box-like/WD repeat-containing protein TBL1XR1	8	29	-0.01	-0.14	-0.26			

Q86WN1	FCH and double SH3 domains protein 1	7	24	-0.15	0.02	0.02			
O94868	FCH and double SH3 domains protein 2	1	1	-0.08	-0.12	-0.05			
O14526	FCH domain only protein 1	4	9	0.27	-0.15	-0.37			
Q9BZ67	FERM domain-containing protein 8	1	1	-0.26	0.51	0.77			
Q86UX7	Fermitin family homolog 3	20	146	0.08	0.40	0.26			
P02794	Ferritin heavy chain	6	19	0.85	0.80	0.16	4		4
P02792	Ferritin light chain	4	12	0.52	1.05	0.41			4
P22830	Ferrochelatase, mitochondrial	8	13	-0.16	0.07	0.31			
O95684	FGFR1 oncogene partner	2	2	-0.43	-0.04	0.40			
Q9NVK5	FGFR1 oncogene partner 2	5	32	-0.36	0.09	0.28			
Q9Y613	FH1/FH2 domain-containing protein 1	5	8	0.08	0.14	0.16			
P02671	Fibrinogen alpha chain	11	27	-0.24	-0.16	0.11			
P02675	Fibrinogen beta chain	4	5	-0.26	-0.04	0.22			
P02679	Fibrinogen gamma chain	5	18	-0.15	-0.11	0.02			
P22607	Fibroblast growth factor receptor 3	1	1	0.21	0.42	0.19			
P02751	Fibronectin	1	1	1.02	1.28	0.27			
Q9BTV5	Fibronectin type III and SPRY domain-containing protein 1	2	4	-0.75	0.30	1.03			
Q9Y2H6	Fibronectin type-III domain-containing protein 3A	3	5	0.25	0.12	-0.04			
P20930	Filaggrin	9	19	0.04	-0.45	-0.58			
Q5D862	Filaggrin-2	5	8	0.24	-1.31	-1.38			
P21333	Filamin-A	144	2187	-0.23	0.43	0.74			4
O75369	Filamin-B	67	321	0.31	-0.33	-0.47			5
Q5T1M5	FK506-binding protein 15	14	47	-0.20	0.11	0.27			
P39748	Flap endonuclease 1	12	51	-0.43	-0.10	0.56			
P30043	Flavin reductase (NADPH)	7	64	-0.19	0.06	0.26			
O75955	Flotillin-1	23	98	-0.33	0.06	0.39			
Q14254	Flotillin-2	21	96	-0.32	0.05	0.25			
Q96SL8	Flt3-interacting zinc finger protein 1	1	1	-0.64	-0.09	0.56			
Q96CP2	FLYWCH family member 2	9	32	-0.24	-0.50	-0.29		4	
Q9P0K8	Forkhead box protein J2	1	2	NA	NA	NA			
P85037	Forkhead box protein K1	8	25	0.12	-0.19	-0.31			
Q01167	Forkhead box protein K2	1	3	-0.16	0.13	0.28			
O43524	Forkhead box protein O3	1	1	-0.22	0.17	0.39			
Q9H334	Forkhead box protein P1	2	8	-0.13	-1.00	-0.80		4	4
Q96RU3	Formin-binding protein 1	22	119	0.35	0.27	-0.08			
Q8N3X1	Formin-binding protein 4	7	26	-0.17	-0.14	-0.11			
O95466	Formin-like protein 1	30	117	0.16	0.50	0.45		4	
P15408	Fos-related antigen 2	5	8	0.22	0.79	0.76			
Q13642	Four and a half LIM domains protein 1	1	5	1.03	0.90	-0.39	3		
Q13643	Four and a half LIM domains protein 3	2	16	-0.47	0.61	0.77		3	5
Q06787	Fragile X mental retardation protein 1	10	19	-0.33	0.23	0.47			4
P51114	Fragile X mental retardation syndrome-related protein 1	5	24	0.00	0.01	-0.18			
P51116	Fragile X mental retardation syndrome-related protein 2	4	8	-0.37	-0.01	0.36			
Q16595	Fra1axin, mitochondrial	2	4	-0.25	-0.37	-0.14			
Q01543	Friend leukemia integration 1 transcription factor	6	20	0.04	0.05	0.16			
Q9H479	Fructosamine-3-kinase	3	4	-0.15	-0.57	-0.42			
P09467	Fructose-1,6-bisphosphatase 1	10	49	-0.09	-0.19	-0.22			
Q9NQ88	Fructose-2,6-bisphosphatase TIGAR	6	17	-0.24	0.02	0.21			
P04075	Fructose-bisphosphate aldolase A	27	735	-0.07	-0.24	-0.20			
P09972	Fructose-bisphosphate aldolase C	21	310	0.01	-0.30	-0.20			
Q8N612	FTS and Hook-interacting protein	1	1	-0.29	0.28	0.55			
A2VDF0	Fucose mutarotase	1	1	0.17	0.39	0.20			
P07954	Fumarate hydratase, mitochondrial	20	86	0.00	-0.16	-0.02			
P16930	Fumarylacetoacetase	4	11	-0.19	0.11	0.25			
Q96GK7	Fumarylacetoacetate hydrolase domain-containing protein 2A	6	20	0.02	-0.06	-0.09			
Q9BWH2	FUN14 domain-containing protein 2	4	13	-0.02	0.17	0.04			
O15117	FYN-binding protein	22	188	-0.55	-1.04	-0.54		5	
Q9BQS8	FYVE and coiled-coil domain-containing protein 1	8	15	0.09	0.14	0.08			
P98174	FYVE, RhoGEF and PH domain-containing protein 1	1	12	1.31	2.10	0.80			
Q5JSP0	FYVE, RhoGEF and PH domain-containing protein 3	13	51	-0.02	-0.23	-0.04			
Q92917	G patch domain and KOW motifs-containing protein	6	16	-0.02	-0.02	0.07			
Q9BRR8	G patch domain-containing protein 1	2	8	-0.18	-0.25	-0.19			
Q8N954	G patch domain-containing protein 11	3	10	-0.20	0.03	0.23			
Q9UKJ3	G patch domain-containing protein 8	12	20	-0.19	-0.07	0.20			
P43250	G protein-coupled receptor kinase 6	5	16	-0.17	0.02	0.02			
Q6ZVF9	G protein-regulated inducer of neurite outgrowth 3	12	33	0.45	1.03	0.39		5	
Q06546	GA-binding protein alpha chain	3	7	0.00	0.13	0.11			
Q06547	GA-binding protein subunit beta-1	3	4	-1.52	-1.03	0.44			
Q8TAK5	GA-binding protein subunit beta-2	3	5	-0.13	-0.44	-0.31			
P54803	Galactocerebrosidase	4	7	-0.14	0.35	0.62			
P51570	Galactokinase	10	46	0.00	0.08	0.03			
P07902	Galactose-1-phosphate uridylyltransferase	6	21	-0.05	0.14	0.17			
P09382	Galectin-1	10	113	-1.25	-0.22	1.29	5		4
Q05315	Galectin-10	1	1	-1.27	0.02	1.30			
P17931	Galectin-3	5	27	1.19	1.49	0.05	5		5
Q08380	Galectin-3-binding protein	3	3	0.80	-0.31	-1.10			
P47929	Galectin-7	1	5	0.95	0.81	-0.14			
O00214	Galectin-8	2	5	0.68	0.62	-0.05			
O00182	Galectin-9	2	4	-1.05	-0.03	1.02			
Q9UEY8	Gamma-adducin	11	28	-0.08	-0.03	-0.23			
P09104	Gamma-enolase	12	154	0.82	-0.17	-0.92	5		5
Q92820	Gamma-glutamyl hydrolase	5	12	-0.61	0.04	0.45			
Q9BVM4	Gamma-glutamylaminocyclotransferase	1	14	-0.40	-0.03	0.35			
O75223	Gamma-glutamylcyclotransferase	8	23	0.02	-0.04	-0.06			
P13284	Gamma-interferon-inducible lysosomal thiol reductase	1	5	-1.02	0.37	1.28			
Q16666	Gamma-interferon-inducible protein 16	37	189	-0.17	0.22	0.34			

Q9HBI0	Gamma-parvin	3	16	-0.08	0.44	0.51			
Q99747	Gamma-soluble NSF attachment protein	9	23	0.00	0.03	0.13			
Q9NUQ3	Gamma-taxilin	3	10	0.47	-0.08	-0.47			
Q9BSJ2	Gamma-tubulin complex component 2	3	4	-0.13	0.03	-0.15			
Q96CW5	Gamma-tubulin complex component 3	5	10	0.05	-0.24	-0.15			
Q96RT7	Gamma-tubulin complex component 6	3	9	-0.18	-0.16	0.15			
P17900	Ganglioside GM2 activator	2	3	-0.10	-0.01	0.09			
Q96QA5	Gasdermin-A	3	4	0.13	0.08	-0.32			
P57764	Gasdermin-D	4	9	-0.21	0.03	0.22			
P16383	GC-rich sequence DNA-binding factor 2	2	2	-0.42	-0.56	-0.13			
O95479	GDH/6PGL endoplasmic bifunctional protein	5	11	-0.34	0.11	0.38			
Q13630	GDP-L-fucose synthase	6	33	0.02	0.19	0.09			
O60547	GDP-mannose 4,6 dehydratase	3	3	-0.03	0.04	0.06			
P06396	Gelsolin	26	151	-1.98	-0.11	1.96	5		5
O14893	Gem-associated protein 2	1	2	0.21	0.07	-0.14			
P57678	Gem-associated protein 4	2	7	0.17	-0.29	-0.45			
Q8TEQ6	Gem-associated protein 5	5	18	0.27	-0.12	-0.44			
Q9P107	GEM-interacting protein	18	56	0.04	0.11	0.14			
Q12789	General transcription factor 3C polypeptide 1	4	4	-0.09	0.04	0.15			
Q8WUA4	General transcription factor 3C polypeptide 2	1	4	-0.31	-0.09	0.22			
Q9Y5Q9	General transcription factor 3C polypeptide 3	2	7	-0.37	-0.14	-0.15			
Q9UKN8	General transcription factor 3C polypeptide 4	4	10	-0.20	-0.05	0.31			
Q9Y5Q8	General transcription factor 3C polypeptide 5	5	11	-0.31	0.05	0.32			
P29083	General transcription factor IIE subunit 1	2	3	-0.01	-0.09	-0.06			
P35269	General transcription factor IIF subunit 1	8	27	0.08	0.13	0.00			
P13984	General transcription factor IIF subunit 2	3	7	-0.37	0.06	0.49			
Q13888	General transcription factor IIH subunit 2	2	2	0.54	-0.18	-0.71			
Q13889	General transcription factor IIH subunit 3	1	1	-0.17	-0.52	-0.36			
Q92759	General transcription factor IIH subunit 4	1	1	-0.49	-0.04	0.43			
P78347	General transcription factor II-I	20	81	-0.07	-0.07	-0.06			
O60763	General vesicular transport factor p115	25	137	0.05	0.31	0.28			
Q14687	Genetic suppressor element 1	1	4	-0.51	0.01	0.28			
Q9NQX3	Gephyrin	1	6	0.45	0.08	-0.34			
P53609	Geranylgeranyl transferase type-1 subunit beta	1	1	NA	NA	NA			
Q92696	Geranylgeranyl transferase type-2 subunit alpha	5	12	0.01	0.23	0.23			
P53611	Geranylgeranyl transferase type-2 subunit beta	1	1	0.18	-0.29	-0.47			
O60318	Germlinal-center associated nuclear protein	5	8	-0.09	0.05	0.15			
Q8N2G8	GH3 domain-containing protein	2	3	-0.25	-0.34	-0.07			
P60983	Glia maturation factor beta	5	51	-0.27	0.11	0.29			
O60234	Glia maturation factor gamma	8	126	-0.02	-0.11	-0.13			
Q9NZM4	Glioma tumor suppressor candidate region gene 1 protein	2	3	-0.76	-0.17	0.60			
Q9NZM5	Glioma tumor suppressor candidate region gene 2 protein	2	4	0.67	0.18	-0.48			
Q92990	Glomulin	1	3	0.08	0.22	0.12			
Q9Y692	Glucocorticoid modulatory element-binding protein 1	3	6	-1.21	-0.61	0.61			
Q9UKD1	Glucocorticoid modulatory element-binding protein 2	3	9	-0.05	-0.08	-0.02			
P04150	Glucocorticoid receptor	7	23	-0.22	0.08	0.45			
Q86VQ1	Glucocorticoid-induced transcript 1 protein	2	3	-0.67	0.28	0.96			
Q96EK6	Glucosamine 6-phosphate N-acetyltransferase	1	2	-0.36	-0.17	0.18			
P46926	Glucosamine-6-phosphate isomerase 1	6	84	0.98	0.48	-0.23	3		
Q8TDQ7	Glucosamine-6-phosphate isomerase 2	2	45	0.34	0.07	-0.27			
Q6PCE3	Glucose 1,6-bisphosphate synthase	1	1	0.20	0.16	-0.04			
P11413	Glucose-6-phosphate 1-dehydrogenase	22	191	-0.69	0.35	0.90	3		4
P06744	Glucose-6-phosphate isomerase	18	209	0.45	0.14	-0.48			
P14314	Glucosidase 2 subunit beta	16	162	-0.42	0.13	0.44			
Q6ZQY3	Glutamate decarboxylase-like protein 1	1	2	NA	NA	NA			
P00367	Glutamate dehydrogenase 1, mitochondrial	28	274	0.19	0.19	0.05			
P48506	Glutamate--cysteine ligase catalytic subunit	7	18	0.07	0.03	-0.01			
P48507	Glutamate--cysteine ligase regulatory subunit	2	11	0.01	0.31	0.49			
Q9BQ67	Glutamate-rich WD repeat-containing protein 1	3	12	0.10	-0.14	-0.21			
O94925	Glutaminase kidney isoform, mitochondrial	12	54	0.40	0.18	-0.25			
P15104	Glutamine synthetase	1	1	1.35	1.28	-0.06			
Q6IA69	Glutamine-dependent NAD(+) synthetase	3	3	0.20	0.37	0.18			
Q06210	Glutamine--fructose-6-phosphate aminotransferase 1	9	35	0.22	0.22	-0.03			
Q2TAL8	Glutamine-rich protein 1	5	10	0.02	0.04	0.04			
P47897	Glutamine--tRNA ligase	8	20	-0.12	0.12	0.24			
Q9NXS2	Glutamyl-peptide cyclotransferase-like protein	1	1	-0.50	-0.10	0.41			
O43716	Glutamyl-tRNA(Gln) amidotransferase subunit C, mitochondrial	1	5	0.19	-0.01	-0.37			
P35754	Glutaredoxin-1	6	80	0.26	0.25	0.27			
O76003	Glutaredoxin-3	4	14	0.29	0.08	-0.09			
Q86SX6	Glutaredoxin-related protein 5, mitochondrial	4	21	-0.24	0.09	0.15			
Q92947	Glutaryl-CoA dehydrogenase, mitochondrial	8	56	0.27	0.06	-0.12			
P07203	Glutathione peroxidase 1	7	21	0.38	-0.31	-0.78			4
Q96SL4	Glutathione peroxidase 7	1	7	NA	NA	NA			
P00390	Glutathione reductase, mitochondrial	20	122	0.06	0.28	0.15			
Q9Y2Q3	Glutathione S-transferase kappa 1	13	104	0.45	0.11	-0.41			
P09488	Glutathione S-transferase Mu 1	3	20	0.51	-0.55	-1.06			
P28161	Glutathione S-transferase Mu 2	2	26	-1.10	-1.11	-0.01			
P78417	Glutathione S-transferase omega-1	11	109	0.39	0.20	-0.12			
P09211	Glutathione S-transferase P	10	169	-1.51	-0.39	0.94	4		4
P30711	Glutathione S-transferase theta-1	3	4	0.08	-0.44	-0.53			
P48637	Glutathione synthetase	17	64	-0.05	-0.14	-0.19			
P04406	Glyceraldehyde-3-phosphate dehydrogenase	30	1622	0.12	-0.04	-0.22			
P32189	Glycerol kinase	2	2	-0.02	0.00	0.02			
Q8N335	Glycerol-3-phosphate dehydrogenase 1-like protein	7	15	1.07	1.14	-0.03	4		4
P43304	Glycerol-3-phosphate dehydrogenase, mitochondrial	11	27	-0.16	0.07	0.34			
Q9NPB8	Glycerophosphocholine phosphodiesterase GPCPD1	1	2	-0.26	0.22	0.48			

P23434	Glycine cleavage system H protein, mitochondrial	1	3	-0.04	-0.14	-0.09			
P41250	Glycine--tRNA ligase	15	42	-0.03	-0.01	-0.13			
P35573	Glycogen debranching enzyme	18	47	0.01	-0.19	-0.30			
P11216	Glycogen phosphorylase, brain form	20	80	-0.02	-0.38	-0.35			
P11217	Glycogen phosphorylase, muscle form	1	9	0.03	-0.16	-0.19			
P49840	Glycogen synthase kinase-3 alpha	4	21	-0.07	0.07	0.14			
P49841	Glycogen synthase kinase-3 beta	1	2	NA	NA	NA			
P13807	Glycogen synthase, muscle	2	6	0.41	0.54	0.13			
P46976	Glycogenin-1	9	57	0.76	1.07	0.42	4		5
Q9NZD2	Glycolipid transfer protein	2	7	-0.28	0.28	0.42			
P04921	Glycophorin-C	1	5	0.11	-0.12	-0.22			
O43292	Glycosylphosphatidylinositol anchor attachment 1 protein	1	3	-0.16	0.02	0.18			
P30419	Glycylpeptide N-tetradecanoyltransferase 1	7	77	0.36	-0.13	-0.45			4
O60551	Glycylpeptide N-tetradecanoyltransferase 2	7	38	0.66	0.06	-0.56	5		4
Q9HC38	Glyoxalase domain-containing protein 4	15	124	0.22	-0.08	-0.43			
Q9UBQ7	Glyoxylate reductase/hydroxypyruvate reductase	12	97	0.02	-0.17	-0.28			
Q9P2T1	GMP reductase 2	10	28	0.33	0.12	-0.16			
P49915	GMP synthase	14	66	0.03	-0.10	0.05			
Q92896	Golgi apparatus protein 1	4	5	-0.35	-0.26	0.27			
O00461	Golgi integral membrane protein 4	1	1	-1.93	-0.92	1.02			
Q9H4A6	Golgi phosphoprotein 3	4	7	0.11	-0.13	0.36			
Q9H4A5	Golgi phosphoprotein 3-like	1	2	0.08	0.51	0.42			
Q9H8Y8	Golgi reassembly-stacking protein 2	3	22	0.21	0.16	0.03			
Q9H3P7	Golgi resident protein GCP60	6	22	0.05	0.20	0.12			
Q95249	Golgi SNAP receptor complex member 1	1	12	0.01	0.21	0.19			
Q7L5D6	Golgi to ER traffic protein 4 homolog	1	1	-0.05	-0.38	-0.32			
Q9HD26	Golgi-associated PDZ and coiled-coil motif-containing protein	1	3	-0.24	0.06	0.31			
Q9H4G4	Golgi-associated plant pathogenesis-related protein 1	7	68	-0.85	0.56	1.39	5		5
Q08379	Golgin subfamily A member 2	8	16	-0.29	-0.02	0.34			
Q08378	Golgin subfamily A member 3	28	87	-0.02	-0.18	-0.07			
Q13439	Golgin subfamily A member 4	10	13	0.08	0.16	0.10			
Q8TBA6	Golgin subfamily A member 5	6	9	-0.21	0.06	0.28			
A6NP81	Golgin subfamily A member 8-like protein 2	4	4	-1.44	-0.01	1.44			
Q14789	Golgin subfamily B member 1	11	15	0.28	0.16	0.01			
Q92538	Golgi-specific brefeldin A-resistance guanine nucleotide exchange factor 1	6	17	-0.05	0.18	0.15			
Q8IXQ4	GPALPP motifs-containing protein 1	2	20	-0.23	-0.32	-0.22			
Q8TEQ8	GPI ethanolamine phosphate transferase 3	1	1	0.01	0.10	0.09			
Q96S52	GPI transamidase component PIG-S	1	3	-0.33	0.03	0.34			
Q969N2	GPI transamidase component PIG-T	3	8	-0.17	0.35	0.59			
Q92643	GPI-anchor transamidase	1	1	-0.19	0.01	0.20			
Q9HCN4	GNP-loop GTPase 1	2	10	0.26	0.11	-0.10			
Q9Y653	G-protein coupled receptor 56	3	13	-0.92	-0.18	0.63	5		5
P28676	Grancalcin	2	2	0.42	-0.86	-1.28			
P28799	Granulins	1	1	-0.02	-0.03	-0.03			
P22749	Granulysin	4	15	-1.82	0.28	2.13	4		4
P12544	Granzyme A	18	164	-0.08	1.60	1.78		5	4
P10144	Granzyme B	5	28	-2.08	0.05	1.82	5		5
P20718	Granzyme H	7	55	-2.44	-0.71	1.64	5		5
P49863	Granzyme K	14	126	1.66	1.91	0.29	5		5
P51124	Granzyme M	7	32	-0.84	0.92	1.90	4		4
Q13588	GRB2-related adapter protein	2	3	-0.06	-1.24	-1.17			
O75791	GRB2-related adapter protein 2	9	69	0.38	0.01	-0.53			5
Q12849	G-rich sequence factor 1	4	17	0.04	-0.01	-0.06			
Q96CN9	GRIP and coiled-coil domain-containing protein 1	5	6	0.14	0.14	0.01			
Q8IWJ2	GRIP and coiled-coil domain-containing protein 2	6	16	-0.05	0.00	-0.04			
Q4V328	GRIP1-associated protein 1	11	25	-0.26	-0.03	0.27			
Q8TAE8	Growth arrest and DNA damage-inducible proteins-interacting protein 1	3	10	-0.47	-0.28	0.23			
O60861	Growth arrest-specific protein 7	1	1	NA	NA	NA			
P62993	Growth factor receptor-bound protein 2	11	52	0.08	-0.23	-0.44			
Q9H3K2	Growth hormone-inducible transmembrane protein	2	3	0.55	0.31	-0.24			
Q9HAV7	GrpE protein homolog 1, mitochondrial	11	25	0.13	-0.09	-0.14			
Q9P0R6	GSK3-beta interaction protein	1	1	0.25	0.03	-0.21			
P30047	GTP cyclohydrolase 1 feedback regulatory protein	2	19	-0.23	0.65	0.78		5	3
Q9UIJ7	GTP:AMP phosphotransferase AK3, mitochondrial	12	61	0.05	-0.21	-0.35			
O75616	GTPase Era, mitochondrial	2	2	0.02	0.03	-0.01			
Q8WWP7	GTPase IMAP family member 1	15	174	0.24	0.15	-0.11			
Q9UG22	GTPase IMAP family member 2	3	10	0.06	0.42	0.36			
Q9NUV9	GTPase IMAP family member 4	23	226	0.82	0.14	-0.69	5		5
Q96F15	GTPase IMAP family member 5	11	47	0.23	0.22	0.02			
Q6P9H5	GTPase IMAP family member 6	1	26	0.09	0.07	-0.01			
Q8NHV1	GTPase IMAP family member 7	8	59	0.16	-0.20	-0.38			
Q8ND71	GTPase IMAP family member 8	17	86	0.13	-0.13	-0.28			
P01116	GTPase KRas	1	44	-0.03	0.02	0.05			
P01111	GTPase NRas	1	41	0.10	0.01	-0.08			
Q14C86	GTPase-activating protein and VPS9 domain-containing protein 1	8	21	-0.02	0.03	0.06			
P62826	GTP-binding nuclear protein Ran	12	172	0.37	-0.03	-0.40			
O00178	GTP-binding protein 1	7	27	0.04	0.21	0.12			
A4D1E9	GTP-binding protein 10	1	1	-0.38	-0.46	-0.07			
Q15382	GTP-binding protein Rheb	3	3	0.07	0.25	0.31			
Q9NR31	GTP-binding protein SAR1a	3	15	0.15	0.28	0.02			
P47224	Guanine nucleotide exchange factor MSS4	1	3	NA	NA	NA			
P04899	Guanine nucleotide-binding protein G(i) subunit alpha-2	9	145	0.11	0.34	0.03			
P59768	Guanine nucleotide-binding protein G(I)/G(S)/G(O) subunit gamma-2	6	14	0.37	0.92	0.46			3
P63218	Guanine nucleotide-binding protein G(I)/G(S)/G(O) subunit gamma-5	2	3	0.26	-0.01	-0.26			
P62873	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-1	4	76	0.28	0.39	0.08			
P62879	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-2	4	56	0.39	0.52	0.13		5	

P08754	Guanine nucleotide-binding protein G(k) subunit alpha	5	88	0.47	0.58	0.10		4	
P09471	Guanine nucleotide-binding protein G(o) subunit alpha	1	59	0.82	0.19	-0.62			
P50148	Guanine nucleotide-binding protein G(q) subunit alpha	2	2	-0.30	-0.18	0.11			
P63092	Guanine nucleotide-binding protein G(s) subunit alpha isoforms short	5	68	0.76	0.67	-0.09	5	5	
Q14344	Guanine nucleotide-binding protein subunit alpha-13	7	88	0.08	0.64	0.60		4	4
P63244	Guanine nucleotide-binding protein subunit beta-2-like 1	16	115	0.37	0.28	-0.40			
P36915	Guanine nucleotide-binding protein-like 1	12	57	0.67	0.16	-0.44	4		
Q9BV2	Guanine nucleotide-binding protein-like 3	13	53	0.52	-0.11	-0.53			5
Q8N4P3	Guanosine-3',5'-bis(diphosphate) 3'-pyrophosphohydrolase MESH1	4	15	-0.18	-0.62	-0.26		4	
Q16774	Guanylate kinase	5	36	-0.10	0.10	0.06			
Q96PP9	Guanylate-binding protein 4	5	24	-0.12	-0.29	-0.16			
Q96PP8	Guanylate-binding protein 5	9	57	0.03	0.77	0.66		5	5
Q8N8V2	Guanylate-binding protein 7	2	9	-0.59	-0.57	0.01			
P51798	H(+)/Cl(-) exchange transporter 7	1	3	-0.59	0.18	0.78			
Q9NY12	H/ACA ribonucleoprotein complex subunit 1	1	3	NA	NA	NA			
Q9NX24	H/ACA ribonucleoprotein complex subunit 2	6	51	0.29	-0.05	-0.30			
Q9NPE3	H/ACA ribonucleoprotein complex subunit 3	6	43	0.27	0.12	-0.20			
O60832	H/ACA ribonucleoprotein complex subunit 4	20	106	0.39	-0.14	-0.54			5
Q9H0R4	Haloacid dehalogenase-like hydrolase domain-containing protein 2	6	38	0.04	-0.61	-0.58		4	
Q9BSH5	Haloacid dehalogenase-like hydrolase domain-containing protein 3	6	21	0.27	-0.06	-0.22			
Q92574	Hamartin	1	1	0.59	0.86	0.28			
Q96CS2	HAUS augmin-like complex subunit 1	2	4	0.10	-0.23	-0.28			
Q9H6D7	HAUS augmin-like complex subunit 4	1	1	-0.05	-0.13	-0.07			
O94927	HAUS augmin-like complex subunit 5	1	1	0.83	0.30	-0.52			
Q7Z4H7	HAUS augmin-like complex subunit 6	2	2	-0.25	-0.34	-0.11			
Q99871	HAUS augmin-like complex subunit 7	1	2	0.17	-0.35	-0.51			
Q9Y450	HBS1-like protein	6	9	0.10	-0.21	-0.25			
Q53T59	HCLS1-binding protein 3	3	5	-0.29	0.01	0.35			
Q7Z4H3	HD domain-containing protein 2	2	8	-0.86	-0.50	0.26	5	5	
Q9UBI9	Headcase protein homolog	4	6	0.02	-0.35	-0.37			
Q9H583	HEAT repeat-containing protein 1	2	3	0.46	-0.24	-0.69			
Q86Y56	HEAT repeat-containing protein 2	1	2	NA	NA	NA			
Q9P2D3	HEAT repeat-containing protein 5B	1	11	-0.15	-0.37	-0.22			
Q6A108	HEAT repeat-containing protein 6	1	1	-0.11	-0.25	-0.14			
P48723	Heat shock 70 kDa protein 13	1	1	-0.09	0.40	0.49			
Q0VDF9	Heat shock 70 kDa protein 14	5	11	0.05	-0.11	-0.23			
P08107	Heat shock 70 kDa protein 1A/1B	24	431	-0.14	-0.10	0.02			
P34932	Heat shock 70 kDa protein 4	32	153	0.17	0.03	-0.09			
P11142	Heat shock cognate 71 kDa protein	34	1129	-0.05	-0.10	-0.08			
Q00613	Heat shock factor protein 1	1	4	NA	NA	NA			
Q92598	Heat shock protein 105 kDa	19	65	-0.01	-0.49	-0.45		5	
Q12931	Heat shock protein 75 kDa, mitochondrial	11	93	0.41	-0.18	-0.66	5		5
P04792	Heat shock protein beta-1	8	24	-0.18	-0.36	-0.16			
P07900	Heat shock protein HSP 90-alpha	26	870	0.23	0.17	-0.25			
P08238	Heat shock protein HSP 90-beta	23	761	0.21	-0.01	-0.13			
Q15477	Helicase SKI2W	12	27	0.26	0.05	-0.29			
Q6ZRS2	Helicase SRCAP	10	14	-0.03	-0.01	-0.01			
Q9BYK8	Helicase with zinc finger domain 2	4	10	-0.17	0.37	0.53			
Q9UK76	Hematological and neurological expressed 1 protein	4	25	-0.78	-0.32	0.38	5		
Q9H910	Hematological and neurological expressed 1-like protein	9	49	0.01	0.04	0.11			
P14317	Hematopoietic lineage cell-specific protein	28	421	-0.10	0.09	0.19			
P09601	Heme oxygenase 1	2	2	-0.97	0.22	1.19			
P30519	Heme oxygenase 2	12	72	-0.09	-0.06	0.11			
Q9NRV9	Heme-binding protein 1	5	6	-0.26	-0.19	0.12			
Q9Y5Z4	Heme-binding protein 2	8	39	0.40	-0.17	-0.31			
Q96RW7	Hemicentin-1	1	5	1.47	1.67	0.29			
P69905	Hemoglobin subunit alpha	11	683	-0.55	-0.66	-0.25		5	
P68871	Hemoglobin subunit beta	8	927	-0.74	-0.76	0.02	5	5	
P02042	Hemoglobin subunit delta	8	463	-0.78	-0.59	0.01	5	5	
P69891	Hemoglobin subunit gamma-1	2	33	-0.90	-0.62	0.09	3	3	
Q9Y251	Heparanase	2	2	-0.45	-0.04	0.41			
O14964	Hepatocyte growth factor-regulated tyrosine kinase substrate	5	16	-0.21	0.08	0.29			
P51858	Hepatoma-derived growth factor	16	132	-0.05	-0.26	-0.24			
Q7Z4V5	Hepatoma-derived growth factor-related protein 2	5	19	-0.04	-0.37	0.01			
Q9NQG7	Hermansky-Pudlak syndrome 4 protein	1	1	-0.38	-0.06	0.32			
Q86YV9	Hermansky-Pudlak syndrome 6 protein	3	5	-0.07	0.04	0.14			
Q5SSJ5	Heterochromatin protein 1-binding protein 3	28	294	0.25	-0.33	-0.49			
Q99729	Heterogeneous nuclear ribonucleoprotein A/B	10	148	-0.08	0.04	0.05			
Q13151	Heterogeneous nuclear ribonucleoprotein A0	11	176	-0.40	-0.25	0.04			
P09651	Heterogeneous nuclear ribonucleoprotein A1	14	387	-0.12	-0.14	0.06			
P51991	Heterogeneous nuclear ribonucleoprotein A3	14	232	-0.14	-0.19	-0.02			
Q14103	Heterogeneous nuclear ribonucleoprotein D0	15	353	-0.22	-0.22	0.06			
O14979	Heterogeneous nuclear ribonucleoprotein D-like	10	200	-0.49	-0.37	0.02			
P52597	Heterogeneous nuclear ribonucleoprotein F	16	204	-0.08	-0.20	-0.03			
P31943	Heterogeneous nuclear ribonucleoprotein H	9	266	0.08	-0.19	-0.08			
P55795	Heterogeneous nuclear ribonucleoprotein H2	9	188	-0.16	-0.05	0.00			
P31942	Heterogeneous nuclear ribonucleoprotein H3	12	161	-0.06	-0.38	-0.31			
P61978	Heterogeneous nuclear ribonucleoprotein K	28	735	-0.14	-0.24	-0.04			
P14866	Heterogeneous nuclear ribonucleoprotein L	20	320	-0.01	-0.20	-0.02			
Q8WV9	Heterogeneous nuclear ribonucleoprotein L-like	4	16	0.59	0.52	-0.32			
P52272	Heterogeneous nuclear ribonucleoprotein M	49	904	-0.17	-0.16	0.12			
O60506	Heterogeneous nuclear ribonucleoprotein Q	17	194	0.06	0.00	-0.06			
O43390	Heterogeneous nuclear ribonucleoprotein R	21	259	-0.08	-0.15	-0.05			
Q00839	Heterogeneous nuclear ribonucleoprotein U	31	372	-0.12	-0.17	0.04			
Q9BUJ2	Heterogeneous nuclear ribonucleoprotein U-like protein 1	18	117	-0.02	0.07	-0.04			
Q1KMD3	Heterogeneous nuclear ribonucleoprotein U-like protein 2	33	247	-0.05	-0.10	-0.03			

P22626	Heterogeneous nuclear ribonucleoproteins A2/B1	28	873	-0.33	-0.33	0.06			
P07910	Heterogeneous nuclear ribonucleoproteins C1/C2	21	626	0.02	-0.17	-0.18			
Q9NZJ6	Hexaprenyldihydroxybenzoate methyltransferase, mitochondrial	1	1	0.15	-0.07	-0.22			
P19367	Hexokinase-1	35	292	0.72	0.27	-0.55	5		5
P52789	Hexokinase-2	2	64	0.53	0.07	-0.45			
P52790	Hexokinase-3	3	12	-0.09	0.03	0.12			
P30273	High affinity immunoglobulin epsilon receptor subunit gamma	4	15	-2.14	0.13	2.09	5		5
Q15651	High mobility group nucleosome-binding domain-containing protein 3	2	3	-2.52	-1.80	0.73			
O00479	High mobility group nucleosome-binding domain-containing protein 4	4	33	0.27	-0.19	-0.46			
P82970	High mobility group nucleosome-binding domain-containing protein 5	2	2	-0.34	0.25	0.60			
Q9NP66	High mobility group protein 20A	2	5	0.05	0.16	0.12			
P09429	High mobility group protein B1	8	108	-0.05	-0.19	-0.30			
P26583	High mobility group protein B2	7	100	-0.07	0.05	0.22			
O15347	High mobility group protein B3	2	3	-0.64	-0.12	0.53			
P17096	High mobility group protein HMG-I/HMG-Y	3	18	0.31	-0.56	-0.45		3	
P37235	Hippocalcin-like protein 1	2	17	0.38	0.19	-0.17			
Q9BW71	HIRA-interacting protein 3	1	3	-0.03	-0.25	-0.28			
O95568	Histidine protein methyltransferase 1 homolog	1	63	0.49	0.35	-0.12			
P49773	Histidine triad nucleotide-binding protein 1	8	75	0.36	0.19	-0.59			4
Q9BX68	Histidine triad nucleotide-binding protein 2, mitochondrial	7	58	-0.21	0.09	0.31			
P12081	Histidine-tRNA ligase, cytoplasmic	13	67	-0.08	-0.04	-0.09			
Q92831	Histone acetyltransferase KAT2B	1	2	-0.16	0.01	0.18			
Q92993	Histone acetyltransferase KAT5	1	2	NA	NA	NA			
Q92794	Histone acetyltransferase KAT6A	5	6	-0.08	-0.23	-0.12			
O95251	Histone acetyltransferase KAT7	6	16	0.18	0.05	-0.13			
Q9H726	Histone acetyltransferase KAT8	2	5	-0.14	-0.24	-0.10			
Q09472	Histone acetyltransferase p300	3	8	-0.22	0.02	0.19			
O14929	Histone acetyltransferase type B catalytic subunit	2	18	-0.33	0.05	0.34			
Q9Y294	Histone chaperone ASF1A	2	7	0.25	0.09	-0.35			
Q13547	Histone deacetylase 1	6	38	0.05	-0.11	-0.21			
Q92769	Histone deacetylase 2	3	22	-0.33	-0.42	-0.09			
O15379	Histone deacetylase 3	1	3	-0.02	-0.02	-0.02			
P56524	Histone deacetylase 4	1	3	-0.25	-0.14	0.12			
Q9UQL6	Histone deacetylase 5	1	3	-0.13	0.00	0.13			
Q9UBN7	Histone deacetylase 6	2	3	0.21	0.17	0.00			
Q8WU14	Histone deacetylase 7	4	8	-0.59	-0.42	0.63			
Q9H0E3	Histone deacetylase complex subunit SAP130	8	29	-0.24	-0.11	0.05			
O00422	Histone deacetylase complex subunit SAP18	8	21	-0.14	-0.53	-0.06		3	
O75446	Histone deacetylase complex subunit SAP30	1	1	0.51	1.01	0.52			
Q9HAJ7	Histone deacetylase complex subunit SAP30L	1	3	0.12	-0.27	-0.42			
P07305	Histone H1.0	7	58	-0.22	-2.15	-1.79		5	5
Q02539	Histone H1.1	3	884	-0.49	-0.29	0.28			
P16403	Histone H1.2	8	2638	-0.03	-0.11	0.08			
P16402	Histone H1.3	9	2613	-0.20	-0.70	-0.52		5	
P10412	Histone H1.4	6	2655	-0.10	0.14	0.55			
P16401	Histone H1.5	11	814	-1.37	-0.16	1.32	5		5
Q92522	Histone H1x	13	205	-0.01	-0.42	-0.46		5	
P04908	Histone H2A type 1-B/E	1	1180	0.12	0.07	-0.11			
Q96KK5	Histone H2A type 1-H	2	1250	-0.41	0.16	0.45			
P0C055	Histone H2A.Z	3	425	0.20	-0.06	-0.31			
P16104	Histone H2AX	5	333	-0.98	-0.20	0.82	4		3
Q96A08	Histone H2B type 1-A	1	1817	0.54	0.90	0.37			
P33778	Histone H2B type 1-B	1	2863	-0.10	-0.82	-0.28		5	
P58876	Histone H2B type 1-D	1	2954	-1.02	-0.77	0.34			
P06899	Histone H2B type 1-J	2	2897	0.20	-0.88	-0.42			3
Q99879	Histone H2B type 1-M	1	2950	-1.20	-0.66	1.11	3		
Q5QNW6	Histone H2B type 2-F	2	2957	-0.88	-1.10	-0.06			3
Q8N257	Histone H2B type 3-B	2	2758	-0.74	0.09	0.84			
P68431	Histone H3.1	3	797	-2.29	-0.87	1.31	5	4	5
P84243	Histone H3.3	3	798	-0.42	-0.62	-0.22			
P62805	Histone H4	15	3544	0.21	0.08	0.04			
Q9UPP1	Histone lysine demethylase PHF8	3	8	-0.18	-0.06	0.07			
Q86X55	Histone-arginine methyltransferase CARM1	1	1	0.14	0.02	-0.14			
Q09028	Histone-binding protein RBBP4	4	65	-0.19	-0.09	0.15			
Q16576	Histone-binding protein RBBP7	5	59	-0.15	-0.10	0.09			
Q03164	Histone-lysine N-methyltransferase 2A	20	35	0.15	-0.14	-0.31			
Q9UMN6	Histone-lysine N-methyltransferase 2B	2	2	0.07	-0.22	-0.30			
Q8NEZ4	Histone-lysine N-methyltransferase 2C	2	2	-0.52	-0.13	0.40			
O14686	Histone-lysine N-methyltransferase 2D	1	1	-0.33	-0.14	0.20			
Q8IZD2	Histone-lysine N-methyltransferase 2E	2	4	-0.24	0.02	0.33			
Q9H9B1	Histone-lysine N-methyltransferase EHMT1	2	4	-0.95	-0.26	0.69			
Q96KQ7	Histone-lysine N-methyltransferase EHMT2	2	2	0.03	-0.39	-0.41			
Q92800	Histone-lysine N-methyltransferase EZH1	1	2	-0.23	-0.22	0.01			
O15047	Histone-lysine N-methyltransferase SETD1A	12	40	-0.05	-0.16	0.02			
Q9UP56	Histone-lysine N-methyltransferase SETD1B	2	7	0.08	-0.08	-0.21			
Q9BYW2	Histone-lysine N-methyltransferase SETD2	1	2	-0.49	-0.08	0.42			
Q86TU7	Histone-lysine N-methyltransferase setd3	5	14	-0.33	0.30	0.61			5
Q15047	Histone-lysine N-methyltransferase SETDB1	3	4	0.04	0.27	0.23			
Q53H47	Histone-lysine N-methyltransferase SETMAR	5	6	0.13	-0.05	-0.05			
O43719	HIV Tat-specific factor 1	6	19	0.10	-0.10	-0.18			
P30443	HLA class I histocompatibility antigen, A-1 alpha chain	5	150	-0.21	-0.37	-0.09			
P13746	HLA class I histocompatibility antigen, A-11 alpha chain	1	152	0.47	1.17	0.69			
P05534	HLA class I histocompatibility antigen, A-24 alpha chain	1	145	0.72	0.99	0.27			
P16190	HLA class I histocompatibility antigen, A-33 alpha chain	6	172	0.19	0.36	0.10		5	
P13747	HLA class I histocompatibility antigen, alpha chain E	6	59	0.07	0.07	-0.09			
P30511	HLA class I histocompatibility antigen, alpha chain F	2	6	-0.61	-0.32	0.23			

P30464	HLA class I histocompatibility antigen, B-15 alpha chain	0	175	NA	NA	NA			
P18463	HLA class I histocompatibility antigen, B-37 alpha chain	0	93	NA	NA	NA			
P30481	HLA class I histocompatibility antigen, B-44 alpha chain	3	72	0.40	1.01	0.58			
P30490	HLA class I histocompatibility antigen, B-52 alpha chain	0	149	NA	NA	NA			
P30492	HLA class I histocompatibility antigen, B-54 alpha chain	0	146	NA	NA	NA			
P30493	HLA class I histocompatibility antigen, B-55 alpha chain	0	148	NA	NA	NA			
P01889	HLA class I histocompatibility antigen, B-7 alpha chain	1	104	0.53	0.33	-0.20			
Q31612	HLA class I histocompatibility antigen, B-73 alpha chain	0	76	NA	NA	NA			
Q29718	HLA class I histocompatibility antigen, B-82 alpha chain	0	92	NA	NA	NA			
P30499	HLA class I histocompatibility antigen, Cw-1 alpha chain	0	77	NA	NA	NA			
P30501	HLA class I histocompatibility antigen, Cw-2 alpha chain	1	113	0.18	0.44	0.17			
P04222	HLA class I histocompatibility antigen, Cw-3 alpha chain	0	108	NA	NA	NA			
P30504	HLA class I histocompatibility antigen, Cw-4 alpha chain	1	166	1.37	-0.12	-1.48			
P10321	HLA class I histocompatibility antigen, Cw-7 alpha chain	1	108	-0.12	0.29	0.41			
P04233	HLA class II histocompatibility antigen gamma chain	3	3	-0.42	0.14	0.55			
P04440	HLA class II histocompatibility antigen, DP beta 1 chain	3	3	-0.85	-0.61	0.25			
Q8WY36	HMG box transcription factor BBX	2	2	-0.12	-0.20	-0.09			
Q9UGU5	HMG domain-containing protein 4	1	1	-0.77	-0.10	0.68			
Q9BPY8	Homeodomain-only protein	2	2	-0.08	0.88	0.96			
Q86YZ3	Hornerin	13	38	-0.13	-0.59	-0.22		3	
P51610	Host cell factor 1	33	240	-0.19	-0.07	0.09			
Q9Y5Z7	Host cell factor 2	1	8	0.19	0.10	-0.09			
P50502	Hsc70-interacting protein	15	126	0.13	-0.35	-0.51			
Q9NZL4	Hsp70-binding protein 1	1	1	NA	NA	NA			
Q16543	Hsp90 co-chaperone Cdc37	14	75	0.13	0.06	-0.10			
Q7L3B6	Hsp90 co-chaperone Cdc37-like 1	1	2	-0.06	-0.11	-0.05			
P42858	Huntingtin	6	12	-0.06	0.14	0.27			
O00291	Huntingtin-interacting protein 1	3	3	-0.51	0.08	0.60			
O75146	Huntingtin-interacting protein 1-related protein	11	27	-0.34	-0.30	-0.13			
Q9NX55	Huntingtin-interacting protein K	3	4	-1.21	-0.68	0.49			
Q92839	Hyaluronan synthase 1	1	1	NA	NA	NA			
Q16836	Hydroxyacyl-coenzyme A dehydrogenase, mitochondrial	13	46	0.17	-0.28	-0.09			
Q16775	Hydroxyacylglutathione hydrolase, mitochondrial	7	21	0.07	-0.05	-0.29			
P35914	Hydroxymethylglutaryl-CoA lyase, mitochondrial	7	28	0.16	-0.04	-0.02			
Q01581	Hydroxymethylglutaryl-CoA synthase, cytoplasmic	1	1	-0.38	0.13	0.51			
Q6YN16	Hydroxysteroid dehydrogenase-like protein 2	8	18	0.29	0.19	-0.15			
Q14526	Hypermethylated in cancer 1 protein	1	1	-0.02	0.20	0.22			
P00492	Hypoxanthine-guanine phosphoribosyltransferase	8	48	0.41	-0.04	-0.26			
Q9Y4L1	Hypoxia up-regulated protein 1	24	99	0.14	0.74	0.55		5	
Q9NWT6	Hypoxia-inducible factor 1-alpha inhibitor	1	1	-0.96	-0.57	0.40			
P22304	Iduronate 2-sulfatase	2	5	-1.04	-0.02	0.89	3		3
P01876	Ig alpha-1 chain C region	2	2	0.27	0.26	0.00			
P01857	Ig gamma-1 chain C region	4	21	-0.93	0.62	1.81	3	5	5
P01859	Ig gamma-2 chain C region	3	4	0.00	0.47	0.12			
P01777	Ig heavy chain V-III region TE1	1	2	-0.26	0.27	0.53			
P01765	Ig heavy chain V-III region T1L	1	3	-0.77	-0.06	0.76			
P01834	Ig kappa chain C region	4	29	-1.12	0.19	1.15	5		5
P01593	Ig kappa chain V-I region AG	1	7	-2.19	0.14	2.34			
P01606	Ig kappa chain V-I region OU	2	7	-0.22	0.31	0.53			
P01619	Ig kappa chain V-III region B6	1	5	NA	NA	NA			
P04433	Ig kappa chain V-III region VG (Fragment)	1	1	-1.61	0.37	1.97			
P01625	Ig kappa chain V-IV region Len	2	6	-0.87	0.48	1.40	4		4
P0CG05	Ig lambda-2 chain C regions	4	11	-0.91	0.22	1.10	5		5
Q8WZA9	Immunity-related GTPase family Q protein	7	16	-0.28	-0.16	0.10			
P01591	Immunoglobulin J chain	1	1	-0.04	-0.79	-0.75			
Q93033	Immunoglobulin superfamily member 2	2	5	0.58	-0.36	-0.94			3
Q969P0	Immunoglobulin superfamily member 8	3	5	0.08	-0.29	-0.37			
P78318	Immunoglobulin-binding protein 1	6	32	0.09	-0.02	0.03			
O00629	Importin subunit alpha-3	5	18	-0.05	0.10	-0.08			
O00505	Importin subunit alpha-4	2	20	0.10	0.30	0.15			
P52294	Importin subunit alpha-5	3	18	-0.18	-0.03	0.24			
O60684	Importin subunit alpha-7	4	6	-0.03	0.29	0.29			
Q14974	Importin subunit beta-1	12	119	0.01	0.02	-0.01			
Q9UI26	Importin-11	1	1	-0.07	-0.06	0.02			
Q8TEX9	Importin-4	2	4	0.46	0.09	-0.38			
O00410	Importin-5	14	29	0.09	0.10	-0.07			
Q95373	Importin-7	1	1	0.41	0.16	-0.25			
Q96P70	Importin-9	3	5	0.03	-0.13	-0.17			
Q3SXM5	Inactive hydroxysteroid dehydrogenase-like protein 1	1	1	-0.39	-0.16	0.23			
Q15111	Inactive phospholipase C-like protein 1	1	1	0.37	0.19	-0.17			
Q9UPR0	Inactive phospholipase C-like protein 2	8	12	-0.23	0.02	0.25			
Q8IV63	Inactive serine/threonine-protein kinase VRK3	5	13	-0.23	-0.09	0.05			
Q8NI35	InaD-like protein	1	17	0.86	0.91	0.16	3		3
Q07820	Induced myeloid leukemia cell differentiation protein Mcl-1	1	6	-0.25	0.06	0.26			
Q9Y6Y0	Influenza virus NS1A-binding protein	1	1	-0.31	0.46	0.75			
Q9UK53	Inhibitor of growth protein 1	2	7	-0.27	-0.22	0.07			
Q9NXR8	Inhibitor of growth protein 3	1	2	-0.12	-0.15	-0.03			
O15111	Inhibitor of nuclear factor kappa-B kinase subunit alpha	1	3	NA	NA	NA			
O14920	Inhibitor of nuclear factor kappa-B kinase subunit beta	9	23	-0.02	-0.07	0.06			
Q14164	Inhibitor of nuclear factor kappa-B kinase subunit epsilon	1	2	0.35	0.23	-0.12			
Q9Y2U8	Inner nuclear membrane protein Man1	6	21	-0.09	0.18	0.27			
Q8NBZ0	INO80 complex subunit E	2	8	-0.11	0.06	0.22			
Q15181	Inorganic pyrophosphatase 2	7	54	0.83	0.19	-0.53	5		5
Q9H2U2	Inorganic pyrophosphatase 2, mitochondrial	8	63	0.53	-0.14	-0.58			5
Q9BY32	Inosine triphosphate pyrophosphatase	5	30	-0.19	-0.12	0.17			
P20839	Inosine-5'-monophosphate dehydrogenase 1	7	26	0.08	0.19	-0.04			

P12268	Inosine-5'-monophosphate dehydrogenase 2	20	108	0.18	-0.12	-0.28			
Q14643	Inositol 1,4,5-trisphosphate receptor type 1	2	7	0.07	-0.21	-0.10			
Q14571	Inositol 1,4,5-trisphosphate receptor type 2	7	17	-0.01	-0.03	-0.08			
Q14573	Inositol 1,4,5-trisphosphate receptor type 3	3	8	0.90	0.68	-0.02	3	3	
Q81WB1	Inositol 1,4,5-trisphosphate receptor-interacting protein	1	1	-0.05	0.59	0.65			
Q3MIP1	Inositol 1,4,5-trisphosphate receptor-interacting protein-like 2	1	1	NA	NA	NA			
O43314	Inositol hexakisphosphate and diphosphoinositol-pentakisphosphate kinase	5	8	-0.13	0.25	0.29			
P29218	Inositol monophosphatase 1	10	59	-0.18	-0.10	0.00			
O14732	Inositol monophosphatase 2	1	1	1.36	1.10	-0.25			
P49441	Inositol polyphosphate 1-phosphatase	2	4	-0.49	0.39	0.89			
Q9BT40	Inositol polyphosphate 5-phosphatase K	1	1	-1.09	-0.47	0.63			
Q9NPH2	Inositol-3-phosphate synthase 1	3	4	-0.30	-0.77	-0.46		3	
Q13572	Inositol-tetrakisphosphate 1-kinase	1	2	-0.28	0.20	0.49			
P27987	Inositol-trisphosphate 3-kinase B	11	24	-0.23	-0.27	-0.13			
Q96DU7	Inositol-trisphosphate 3-kinase C	1	2	-0.51	0.22	0.73			
Q9Y4H2	Insulin receptor substrate 2	2	7	-0.47	-0.01	0.38			
Q9Y5U4	Insulin-induced gene 2 protein	1	1	-0.43	-0.05	0.38			
O00425	Insulin-like growth factor 2 mRNA-binding protein 3	1	2	NA	NA	NA			
P18065	Insulin-like growth factor-binding protein 2	1	1	NA	NA	NA			
Q86V85	Integral membrane protein GPR180	1	1	-0.25	-0.11	0.15			
Q8N201	Integrator complex subunit 1	6	15	-0.26	-0.13	0.14			
Q9NVR2	Integrator complex subunit 10	3	5	0.06	-0.15	-0.21			
Q5TA45	Integrator complex subunit 11	1	2	NA	NA	NA			
Q96CB8	Integrator complex subunit 12	4	6	-0.34	-0.08	0.30			
Q9H0H0	Integrator complex subunit 2	1	1	0.24	-0.06	-0.30			
Q68E01	Integrator complex subunit 3	3	17	-0.44	0.06	0.46			
Q96HW7	Integrator complex subunit 4	5	9	0.02	0.03	-0.02			
Q6P9B9	Integrator complex subunit 5	3	7	-0.02	-0.02	-0.13			
Q9UL03	Integrator complex subunit 6	2	3	-0.18	-0.04	0.13			
Q9NVH2	Integrator complex subunit 7	2	4	-0.04	-0.16	-0.08			
Q75QN2	Integrator complex subunit 8	1	3	0.04	-0.02	-0.06			
Q9UKX5	Integrin alpha-11	1	1	0.04	-0.12	-0.15			
P13612	Integrin alpha-4	2	17	-0.01	0.53	0.32		3	
P08648	Integrin alpha-5	3	5	-0.34	0.40	0.65			3
P23229	Integrin alpha-6	4	4	-0.53	-0.12	0.41			
P08514	Integrin alpha-IIb	13	59	-0.10	-0.20	0.02			
P20701	Integrin alpha-L	23	120	-0.31	0.63	0.82		3	4
P11215	Integrin alpha-M	24	124	-2.03	-0.08	1.66	5		5
P20702	Integrin alpha-X	5	16	-1.64	0.12	1.56	3		3
P05556	Integrin beta-1	11	59	-0.31	0.28	0.30			
P05107	Integrin beta-2	25	203	-1.19	0.47	1.54	5		5
P05106	Integrin beta-3	8	25	-0.07	-0.03	-0.06			
P26010	Integrin beta-7	2	7	0.39	0.03	-0.31			
Q969R8	Integrin-alpha FG-GAP repeat-containing protein 2	2	2	0.20	-0.37	-0.57			
Q9H0C8	Integrin-linked kinase-associated serine/threonine phosphatase 2C	10	66	-0.49	-0.28	0.19			
Q13418	Integrin-linked protein kinase	11	59	-0.04	0.35	0.38			
Q8WWN9	Interactor protein for cytohesin exchange factors 1	3	17	0.40	0.02	-0.44			
P19827	Inter-alpha-trypsin inhibitor heavy chain H1	1	1	-0.03	-0.15	-0.14			
P19823	Inter-alpha-trypsin inhibitor heavy chain H2	6	18	0.97	1.07	0.12	3		
Q06033	Inter-alpha-trypsin inhibitor heavy chain H3	1	1	1.52	1.99	0.47			
P05362	Intercellular adhesion molecule 1	3	9	-0.62	0.67	1.13		3	5
P13598	Intercellular adhesion molecule 2	2	12	-0.28	0.28	0.50			4
P32942	Intercellular adhesion molecule 3	12	97	-0.14	0.72	0.91		4	5
P14316	Interferon regulatory factor 2	1	3	NA	NA	NA			
Q8IU81	Interferon regulatory factor 2-binding protein 1	4	7	-0.07	0.02	0.06			
Q7Z5L9	Interferon regulatory factor 2-binding protein 2	3	11	-0.08	0.07	0.24			
Q9H1B7	Interferon regulatory factor 2-binding protein-like	7	25	-0.54	-0.10	0.33			
Q14653	Interferon regulatory factor 3	5	5	-0.01	-0.14	-0.13			
Q92985	Interferon regulatory factor 7	3	10	-0.42	-0.02	0.58			
Q00978	Interferon regulatory factor 9	4	11	-0.47	-0.03	0.44			
P80217	Interferon-induced 35 kDa protein	2	2	0.58	0.04	-0.53			
P20591	Interferon-induced GTP-binding protein Mx1	14	131	0.04	0.21	0.21			
P20592	Interferon-induced GTP-binding protein Mx2	13	119	0.53	0.26	-0.19			
P32455	Interferon-induced guanylate-binding protein 1	12	90	0.61	-0.01	-0.75	4		5
P32456	Interferon-induced guanylate-binding protein 2	13	67	0.73	0.34	-0.41	5		
Q9BYX4	Interferon-induced helicase C domain-containing protein 1	3	5	0.01	0.19	0.18			
P09914	Interferon-induced protein with tetratricopeptide repeats 1	4	20	-0.66	0.23	0.82			
O14879	Interferon-induced protein with tetratricopeptide repeats 3	7	30	-0.74	-0.12	0.66	4		5
Q13325	Interferon-induced protein with tetratricopeptide repeats 5	4	12	-0.16	-0.04	0.14			
P19525	Interferon-induced, double-stranded RNA-activated protein kinase	13	38	0.06	0.18	0.17			
O75569	Interferon-inducible double-stranded RNA-dependent protein kinase activat	7	22	0.31	-0.18	-0.54			5
O00458	Interferon-related developmental regulator 1	1	5	0.07	-0.03	-0.09			
Q9H9L3	Interferon-stimulated 20 kDa exonuclease-like 2	3	5	0.00	-0.05	0.01			
Q96AZ6	Interferon-stimulated gene 20 kDa protein	7	55	0.02	0.05	0.02			
Q12905	Interleukin enhancer-binding factor 2	13	185	0.07	-0.03	-0.17			
Q12906	Interleukin enhancer-binding factor 3	33	284	-0.02	-0.05	-0.13			
P01584	Interleukin-1 beta	2	3	0.20	0.48	0.28			
Q9NWZ3	Interleukin-1 receptor-associated kinase 4	12	44	-0.09	0.10	0.23			
P20809	Interleukin-11	1	1	NA	NA	NA			
Q13478	Interleukin-18 receptor 1	2	2	0.41	0.82	0.41			
P14784	Interleukin-2 receptor subunit beta	1	2	-2.23	0.21	2.45			
Q6UWB1	Interleukin-27 receptor subunit alpha	1	1	NA	NA	NA			
P16871	Interleukin-7 receptor subunit alpha	2	6	2.10	0.93	-1.09	4	4	4
P10145	Interleukin-8	1	1	-1.72	0.00	1.72			
Q15811	Intersectin-1	1	1	-0.45	0.33	0.79			
Q9NZM3	Intersectin-2	13	34	-0.07	0.02	0.22			

Q5JVS0	Intracellular hyaluronan-binding protein 4	2	3	-0.22	-0.54	-0.32			
Q9BW83	Intraflagellar transport protein 27 homolog	4	5	-0.32	0.07	0.38			
O60306	Intron-binding protein aquarius	7	21	-0.12	-0.11	0.11			
Q27J81	Inverted formin-2	3	3	0.16	-0.41	-0.57			
Q6DN90	IQ motif and SEC7 domain-containing protein 1	2	3	-0.32	0.34	0.66			
Q9BUE6	Iron-sulfur cluster assembly 1 homolog, mitochondrial	2	3	0.12	0.19	-0.08			
Q86U28	Iron-sulfur cluster assembly 2 homolog, mitochondrial	5	17	0.42	-0.29	-0.70			5
Q9H1K1	Iron-sulfur cluster assembly enzyme ISCU, mitochondrial	7	22	0.21	-0.16	-0.36			
Q8IWL3	Iron-sulfur cluster co-chaperone protein HscB, mitochondrial	1	2	-0.16	-0.10	0.06			
Q8TB37	Iron-sulfur protein NUBPL	4	7	0.54	0.20	-0.38			
Q2TAA2	Isoamyl acetate-hydrolyzing esterase 1 homolog	6	16	0.25	-0.16	-0.36			
Q9UKU7	Isobutyryl-CoA dehydrogenase, mitochondrial	9	31	0.15	-0.06	-0.18			
Q96CN7	Isochorismatase domain-containing protein 1	7	23	0.14	0.05	-0.11			
Q96AB3	Isochorismatase domain-containing protein 2, mitochondrial	3	3	0.52	0.18	-0.35			
O75874	Isocitrate dehydrogenase cytoplasmic	15	60	0.09	0.23	0.24			
P50213	Isocitrate dehydrogenase subunit alpha, mitochondrial	12	38	0.24	-0.04	-0.41			
O43837	Isocitrate dehydrogenase subunit beta, mitochondrial	11	53	0.32	-0.07	-0.32			
P51553	Isocitrate dehydrogenase subunit gamma, mitochondrial	6	23	0.32	0.06	-0.15			
P48735	Isocitrate dehydrogenase, mitochondrial	27	256	-0.41	0.11	0.40			
P41252	Isoleucine--tRNA ligase, cytoplasmic	11	39	0.16	0.03	0.03			
Q9NSE4	Isoleucine--tRNA ligase, mitochondrial	22	121	0.35	0.13	-0.30			
Q13907	Isopentenyl-diphosphate Delta-isomerase 1	1	1	-0.59	0.15	0.72			
P26440	Isovaleryl-CoA dehydrogenase, mitochondrial	8	42	-0.03	-0.41	-0.47		5	4
P53990	IST1 homolog	6	48	0.02	0.07	-0.08			
Q96N16	Janus kinase and microtubule-interacting protein 1	1	1	0.02	0.28	0.26			
P0C870	JmjC domain-containing protein 7	1	1	NA	NA	NA			
P14923	Junction plakoglobin	3	7	1.01	-0.43	-1.35			
Q9Y624	Junctional adhesion molecule A	4	7	-0.38	-0.21	0.17			
O60229	Kalirin	1	1	0.03	-0.27	-0.32			
Q9BWU0	Kanadaplin	3	8	-0.15	-0.10	0.05			
Q7Z3B3	KAT8 regulatory NSL complex subunit 1	1	1	0.05	0.06	0.02			
Q9H9L4	KAT8 regulatory NSL complex subunit 2	3	5	0.15	-0.03	-0.17			
Q9P2N6	KAT8 regulatory NSL complex subunit 3	1	1	-0.31	0.35	0.68			
Q7Z4H8	KDEL motif-containing protein 2	2	5	-0.23	-0.01	0.18			
Q8TBB5	Kelch domain-containing protein 4	5	7	-0.24	0.11	0.28			
O94819	Kelch repeat and BTB domain-containing protein 11	1	1	NA	NA	NA			
Q8N4N3	Kelch-like protein 36	3	4	-0.10	-0.42	-0.31			
Q92764	Keratin, type I cuticular Ha5	1	6	0.02	0.03	0.01			
P13645	Keratin, type I cytoskeletal 10	21	286	-0.03	-0.06	-0.09			
P13646	Keratin, type I cytoskeletal 13	1	22	0.42	0.57	0.15			
P02533	Keratin, type I cytoskeletal 14	4	90	0.57	0.39	-0.09			
P19012	Keratin, type I cytoskeletal 15	1	36	NA	NA	NA			
P08779	Keratin, type I cytoskeletal 16	9	89	1.54	0.93	-0.02	3		
Q04695	Keratin, type I cytoskeletal 17	8	54	1.15	1.10	-0.14			
P05783	Keratin, type I cytoskeletal 18	1	5	NA	NA	NA			
P35527	Keratin, type I cytoskeletal 9	26	435	0.17	-0.09	-0.13			
P04264	Keratin, type II cytoskeletal 1	35	514	0.05	0.27	0.04			
P35908	Keratin, type II cytoskeletal 2 epidermal	31	330	-0.06	0.00	-0.27			
P12035	Keratin, type II cytoskeletal 3	0	29	NA	NA	NA			
P19013	Keratin, type II cytoskeletal 4	0	29	NA	NA	NA			
P13647	Keratin, type II cytoskeletal 5	17	136	-0.09	-0.23	-0.03			
P02538	Keratin, type II cytoskeletal 6A	5	138	0.58	0.25	0.04			
P04259	Keratin, type II cytoskeletal 6B	2	136	1.38	1.07	-0.35			
Q7RTS7	Keratin, type II cytoskeletal 74	1	21	1.57	1.62	-0.13			
Q8N1N4	Keratin, type II cytoskeletal 78	0	16	NA	NA	NA			
Q5XKE5	Keratin, type II cytoskeletal 79	1	59	2.24	1.32	-0.91			
P05787	Keratin, type II cytoskeletal 8	2	82	NA	NA	NA			
Q6KB66	Keratin, type II cytoskeletal 80	1	4	1.23	0.97	-0.25			
Q5T749	Keratinocyte proline-rich protein	1	1	-1.11	-0.85	0.24			
Q9HA64	Ketosamine-3-kinase	8	19	-0.03	-0.21	-0.13			
Q07666	KH domain-containing, RNA-binding, signal transduction-associated protein	14	143	-0.23	-0.17	0.09			
P43631	Killer cell immunoglobulin-like receptor 2DS2	1	3	-1.51	0.07	1.59			
Q9NZS2	Killer cell lectin-like receptor subfamily F member 1	1	1	-0.34	0.06	0.41			
Q86UP2	Kinectin	34	132	0.07	0.08	-0.11			
O60282	Kinesin heavy chain isoform 5C	4	29	1.78	1.37	-0.41	3		3
Q07866	Kinesin light chain 1	8	32	0.16	0.43	0.15			
Q9H0B6	Kinesin light chain 2	3	17	-0.52	0.34	0.49			
Q9NSK0	Kinesin light chain 4	3	16	-0.14	0.04	0.28			
P33176	Kinesin-1 heavy chain	17	75	-0.20	-0.05	0.25			
Q9NQ78	Kinesin-like protein KIF13B	6	16	-0.37	0.16	0.57			
Q15058	Kinesin-like protein KIF14	1	1	-1.85	1.01	2.87			
Q12756	Kinesin-like protein KIF1A	2	3	0.62	0.44	-0.18			
Q7Z456	Kinesin-like protein KIF21A	3	7	-0.12	0.14	0.17			
O75037	Kinesin-like protein KIF21B	1	4	-0.60	0.24	0.84			
O00139	Kinesin-like protein KIF2A	16	54	0.12	-0.08	-0.19			
Q9Y496	Kinesin-like protein KIF3A	2	2	-0.07	0.05	0.13			
O15066	Kinesin-like protein KIF3B	5	6	0.36	0.33	-0.17			
Q9H410	Kinetochore-associated protein DSN1 homolog	2	5	-0.48	-0.25	0.24			
Q96IY1	Kinetochore-associated protein NSL1 homolog	3	4	0.74	-0.10	-0.85			
P01042	Kininogen-1	1	2	1.46	1.67	0.21			
Q6NY19	KN motif and ankyrin repeat domain-containing protein 3	5	10	-0.94	0.29	1.33	4		4
O00522	Krev interaction trapped protein 1	2	4	0.14	0.35	0.21			
Q13601	KRR1 small subunit processome component homolog	5	9	0.32	-0.13	-0.28			
Q9Y4X4	Krueppel-like factor 12	4	7	-0.19	-0.02	0.17			
Q9Y2Y9	Krueppel-like factor 13	2	5	-0.06	0.08	0.14			
Q9BXX1	Krueppel-like factor 16	1	2	0.32	0.03	-0.29			

Q9Y5W3	Kruppel-like factor 2	1	1	-0.14	-0.81	-0.66			
Q16773	Kynurenine--oxoglutarate transaminase 1	1	7	0.11	-0.25	-0.32			
Q6YP21	Kynurenine--oxoglutarate transaminase 3	5	29	0.38	0.06	-0.28			
Q9H9P8	L-2-hydroxyglutarate dehydrogenase, mitochondrial	3	5	0.36	-0.10	-0.46			
Q8WV93	Lactation elevated protein 1	1	1	0.14	-0.20	-0.34			
P02788	Lactotransferrin	12	22	0.34	0.20	-0.25			
Q04760	Lactoylglutathione lyase	4	51	0.38	0.35	-0.13			
Q9Y252	Lambda-crystallin homolog	3	6	0.50	-0.11	-0.60			
P42166	Lamina-associated polypeptide 2, isoform alpha	12	277	-0.21	-0.37	0.02			
P42167	Lamina-associated polypeptide 2, isoforms beta/gamma	12	431	-0.13	-0.44	-0.30			
Q14739	Lamin-B receptor	6	25	-0.42	-0.18	0.15			
P20700	Lamin-B1	51	804	-0.35	-0.50	-0.26			5
Q03252	Lamin-B2	51	601	0.12	-0.09	-0.18			
Q96RQ9	L-amino-acid oxidase	16	115	1.82	2.00	0.02	5		5
Q9NRN7	L-aminoadipate-serialdehyde dehydrogenase-phosphopantetheinyl transferase	3	4	0.00	-0.07	-0.07			
O43813	LanC-like protein 1	2	20	0.32	-0.12	-0.58			
Q9NS86	LanC-like protein 2	1	4	-0.11	0.12	0.22			
P48449	Lanosterol synthase	1	1	-0.43	-0.27	0.16			
Q6PKG0	La-related protein 1	11	22	0.09	-0.09	-0.08			
Q92615	La-related protein 4B	4	5	-0.24	-0.25	0.34			
Q4G0J3	La-related protein 7	9	39	-0.19	-0.18	0.11			
Q01650	Large neutral amino acids transporter small subunit 1	2	7	2.01	2.38	0.37	5		5
P46379	Large proline-rich protein BAG6	7	22	0.27	-0.06	-0.21			
Q9H089	Large subunit GTPase 1 homolog	4	7	0.05	-0.38	-0.48			
Q9UK59	Lariat debranching enzyme	5	19	0.07	-0.18	-0.22			
Q8NBF6	Late secretory pathway protein AVL9 homolog	2	2	-0.23	-0.45	-0.23			
Q14766	Latent-transforming growth factor beta-binding protein 1	1	1	0.17	-0.24	-0.43			
Q9BS40	Latexin	3	8	-0.28	-0.19	-0.02			
Q9H400	Lck-interacting transmembrane adapter 1	4	15	0.42	-0.01	-0.44			
Q14696	LDLR chaperone MESD	3	9	0.12	0.09	-0.06			
Q99538	Legumain	1	1	-1.97	-0.26	1.72			
Q8NC56	LEM domain-containing protein 2	3	17	-0.03	0.07	0.14			
Q15334	Lethal(2) giant larvae protein homolog 1	2	3	-0.35	0.22	0.62			
Q6P1M3	Lethal(2) giant larvae protein homolog 2	1	2	-0.60	0.20	0.80			
Q96JM7	Lethal(3)malignant brain tumor-like protein 3	5	16	0.09	-0.29	-0.54			
O95202	LETM1 and EF-hand domain-containing protein 1, mitochondrial	9	26	0.01	0.18	0.29			
Q9UIC8	Leucine carboxyl methyltransferase 1	1	3	0.05	0.28	0.12			
Q86V48	Leucine zipper protein 1	8	19	0.37	0.76	0.47		4	4
Q9Y250	Leucine zipper putative tumor suppressor 1	1	2	0.14	-0.05	-0.18			
Q9NQ48	Leucine zipper transcription factor-like protein 1	6	8	0.02	-0.05	-0.02			
P02750	Leucine-rich alpha-2-glycoprotein	1	1	-1.32	-0.74	0.60			
P42704	Leucine-rich PPR motif-containing protein, mitochondrial	27	106	0.46	0.16	-0.43	5		
Q9Y219	Leucine-rich repeat and calponin homology domain-containing protein 1	1	9	-0.25	0.02	0.41			
Q96I18	Leucine-rich repeat and calponin homology domain-containing protein 3	4	20	-0.07	0.01	0.09			
O75427	Leucine-rich repeat and calponin homology domain-containing protein 4	12	50	0.02	-0.17	-0.16			
Q9UFC0	Leucine-rich repeat and WD repeat-containing protein 1	3	5	-0.22	-0.11	0.14			
Q32MZ4	Leucine-rich repeat flightless-interacting protein 1	23	129	0.04	0.04	0.05			
Q9Y608	Leucine-rich repeat flightless-interacting protein 2	4	14	0.24	0.08	0.06			
Q9UQ13	Leucine-rich repeat protein SHOC-2	3	13	-0.10	-0.07	0.07			
Q5S007	Leucine-rich repeat serine/threonine-protein kinase 2	1	5	0.12	-0.10	-0.22			
Q6F5E8	Leucine-rich repeat-containing protein 16C	11	41	0.65	0.12	-0.54	5		4
Q8TCA0	Leucine-rich repeat-containing protein 20	1	1	NA	NA	NA			
Q9H9A6	Leucine-rich repeat-containing protein 40	9	14	-0.02	0.11	0.05			
Q15345	Leucine-rich repeat-containing protein 41	3	5	-0.14	-0.07	0.17			
Q8N1G4	Leucine-rich repeat-containing protein 47	22	151	0.05	-0.13	-0.31			
Q8N9N7	Leucine-rich repeat-containing protein 57	1	5	0.03	0.29	0.18			
Q96AG4	Leucine-rich repeat-containing protein 59	4	8	-0.10	0.48	0.17			
Q96NW7	Leucine-rich repeat-containing protein 7	1	8	-0.45	0.62	1.07			
Q9P2J5	Leucine--tRNA ligase, cytoplasmic	15	35	0.30	-0.06	-0.26			
Q9UIQ6	Leucyl-cystinyl aminopeptidase	4	22	-0.42	-0.12	0.23			
P30740	Leukocyte elastase inhibitor	24	232	-0.54	-0.21	0.23			
Q8NHL6	Leukocyte immunoglobulin-like receptor subfamily B member 1	2	2	0.23	0.04	-0.19			
Q96BZ8	Leukocyte receptor cluster member 1	5	13	0.01	-0.30	-0.16			
Q96B70	Leukocyte receptor cluster member 9	1	1	-0.46	0.20	0.64			
Q08722	Leukocyte surface antigen CD47	4	50	0.32	0.79	0.43			5
P19397	Leukocyte surface antigen CD53	2	3	0.49	0.46	-0.02			
Q6GTX8	Leukocyte-associated immunoglobulin-like receptor 1	3	14	-0.78	0.00	0.61	4		3
P16150	Leukosialin	5	55	-0.38	0.35	0.67			4
P09960	Leukotriene A-4 hydrolase	23	144	0.13	-0.06	-0.35			
O60711	Leupaxin	9	70	0.41	0.13	-0.05			
Q9UNZ5	Leydig cell tumor 10 kDa protein homolog	4	14	-0.03	-0.28	-0.11			
Q8NOW3	L-fucose kinase	2	4	0.17	-0.03	-0.19			
Q8N3X6	Ligand-dependent nuclear receptor corepressor-like protein	1	1	-0.31	1.46	1.79			
Q5T3J3	Ligand-dependent nuclear receptor-interacting factor 1	1	2	-0.20	0.25	0.46			
P48059	LIM and senescent cell antigen-like-containing domain protein 1	2	7	0.11	0.37	0.27			
Q14847	LIM and SH3 domain protein 1	15	348	-0.99	0.13	1.01	5		5
Q9UHB6	LIM domain and actin-binding protein 1	8	16	-0.38	-0.34	0.21			
Q8WWI1	LIM domain only protein 7	4	66	0.15	-0.95	-1.08			3
Q86U70	LIM domain-binding protein 1	2	6	-0.60	-0.16	0.30			
Q9UGP4	LIM domain-containing protein 1	4	15	-0.80	0.12	0.96	5		5
Q9BT23	LIM domain-containing protein 2	3	18	-0.35	-0.32	0.18			
O43561	Linker for activation of T-cells family member 1	3	10	0.70	0.14	-0.50	4		
Q9GZY6	Linker for activation of T-cells family member 2	1	1	-1.42	0.19	1.61			
Q9BU23	Lipase maturation factor 2	3	12	0.14	0.51	0.30			
P11182	Lipoamide acyltransferase component of branched-chain alpha-keto acid dehydrogenase	9	26	0.20	-0.01	-0.19			
Q86X29	Lipolysis-stimulated lipoprotein receptor	1	3	0.75	-0.17	-0.93	3		3

Q93052	Lipoma-preferred partner	8	13	-0.38	0.32	0.79			5
Q99732	Lipopolysaccharide-induced tumor necrosis factor-alpha factor	1	6	-0.52	0.21	0.58			5
P50851	Lipopolysaccharide-responsive and beige-like anchor protein	18	43	0.14	0.16	-0.06			
Q13136	Liprin-alpha-1	4	9	-0.15	0.01	0.08			
Q8ND30	Liprin-beta-2	1	1	-0.66	-0.64	0.02			
P23141	Liver carboxylesterase 1	3	3	0.06	-0.06	0.06			
Q8IVB5	LIX1-like protein	2	2	0.15	-0.21	-0.35			
P00338	L-lactate dehydrogenase A chain	16	214	0.56	0.07	-0.47	4		
P07195	L-lactate dehydrogenase B chain	17	303	0.59	-1.22	-1.79	5	5	5
P36776	Lon protease homolog, mitochondrial	26	87	0.43	0.00	-0.49	5		
Q6PCB7	Long-chain fatty acid transport protein 1	2	2	1.94	0.32	-1.61			
Q5K4L6	Long-chain fatty acid transport protein 3	2	6	-0.46	0.09	0.35			
Q6P1M0	Long-chain fatty acid transport protein 4	2	3	-0.18	0.10	0.21			
O95573	Long-chain-fatty-acid--CoA ligase 3	3	22	-0.13	0.22	0.35			
O60488	Long-chain-fatty-acid--CoA ligase 4	2	8	-0.18	0.08	0.26			
Q9ULC5	Long-chain-fatty-acid--CoA ligase 5	6	11	-0.22	0.19	0.36			
Q969J3	Loss of heterozygosity 12 chromosomal region 1 protein	5	16	0.15	0.09	0.06			
P12318	Low affinity immunoglobulin gamma Fc region receptor II-a	1	2	-0.17	0.06	0.23			
P08637	Low affinity immunoglobulin gamma Fc region receptor III-A	3	10	-2.88	-0.05	2.82	3		3
Q5SW96	Low density lipoprotein receptor adapter protein 1	2	8	-0.02	-0.78	-0.68		5	5
P24666	Low molecular weight phosphotyrosine protein phosphatase	6	33	-0.18	-0.08	0.26			
P14151	L-selectin	2	4	-1.43	-2.34	-0.77		3	
O95232	Luc7-like protein 3	9	15	0.01	-0.11	-0.09			
P05455	Lupus La protein	20	189	0.29	0.05	-0.39			
Q7Z4W1	L-xylulose reductase	10	71	-0.17	-0.48	-0.38			
O95274	Ly6/PLAUR domain-containing protein 3	1	1	NA	NA	NA			
O60449	Lymphocyte antigen 75	2	2	-0.12	0.07	0.20			
Q13094	Lymphocyte cytosolic protein 2	13	75	0.04	0.17	0.07			
P33241	Lymphocyte-specific protein 1	22	269	-0.53	0.00	0.42			
Q9UJU2	Lymphoid enhancer-binding factor 1	3	15	-0.12	-2.09	-1.96		4	4
Q12912	Lymphoid-restricted membrane protein	3	4	-0.30	0.00	0.30			
Q9NU23	LYR motif-containing protein 2	1	3	-0.03	0.06	0.10			
Q9HD34	LYR motif-containing protein 4	1	2	0.39	0.09	-0.30			
A8MSI8	LYR motif-containing protein 9	1	1	0.36	-0.49	-0.84			
P46736	Lys-63-specific deubiquitinase BRCC36	5	13	0.76	-0.10	-0.80	3		3
Q9Y2K7	Lysine-specific demethylase 2A	7	20	-0.18	-0.02	0.04			
Q8NHM5	Lysine-specific demethylase 2B	1	1	-0.27	0.19	0.46			
Q9Y4C1	Lysine-specific demethylase 3A	4	5	-0.27	-0.42	-0.13			
Q7LBC6	Lysine-specific demethylase 3B	9	9	-0.05	-0.18	0.01			
O94953	Lysine-specific demethylase 4B	1	2	-0.88	-0.52	0.37			
Q9H3R0	Lysine-specific demethylase 4C	1	1	-0.17	0.19	0.37			
P29375	Lysine-specific demethylase 5A	6	9	0.11	0.00	0.01			
O15550	Lysine-specific demethylase 6A	2	3	0.30	0.37	0.07			
Q6ZMT4	Lysine-specific demethylase 7A	1	1	-0.23	0.09	0.33			
O75151	Lysine-specific demethylase PHF2	3	10	0.19	0.21	0.03			
O60341	Lysine-specific histone demethylase 1A	9	21	-0.29	-0.13	0.12			
Q15046	Lysine--tRNA ligase	17	65	0.76	0.34	-0.28	5		
Q8IV50	LysM and putative peptidoglycan-binding domain-containing protein 2	4	21	0.18	0.10	-0.10			
Q8NF37	Lysophosphatidylcholine acyltransferase 1	4	12	-0.68	0.94	1.67		4	4
Q5VWZ2	Lysophospholipase-like protein 1	5	11	0.46	-0.14	-0.48			
Q96N66	Lysophospholipid acyltransferase 7	2	2	0.14	0.22	0.07			
Q643R3	Lysophospholipid acyltransferase LPCAT4	2	3	0.91	0.56	-0.11			
P38571	Lysosomal acid lipase/cholesteryl ester hydrolase	1	1	-0.40	-0.46	-0.06			
P11117	Lysosomal acid phosphatase	3	3	-0.25	0.28	0.54			
P10253	Lysosomal alpha-glucosidase	4	23	-0.17	0.25	0.53			5
O00754	Lysosomal alpha-mannosidase	6	15	-0.33	0.14	0.53			
P10619	Lysosomal protective protein	3	20	0.64	0.75	0.24	4	5	
P42785	Lysosomal Pro-X carboxypeptidase	6	31	-1.09	0.16	1.25	3		5
Q99698	Lysosomal-trafficking regulator	2	4	0.05	0.34	0.44			
P11279	Lysosome-associated membrane glycoprotein 1	5	29	-0.54	0.60	0.65		3	5
P13473	Lysosome-associated membrane glycoprotein 2	2	2	-1.76	-0.76	1.00			
P61626	Lysozyme C	6	26	0.13	0.03	0.03			
Q8IU60	m7GpppN-mRNA hydrolase	1	1	NA	NA	NA			
Q96C86	m7GpppX diphosphatase	11	62	-0.13	0.22	0.32			
Q8N5G2	Macoillin	1	1	0.20	0.19	-0.02			
Q7L5Y9	Macrophage erythroblast attacher	2	3	0.06	0.41	0.12			
P14174	Macrophage migration inhibitory factor	2	167	0.21	-0.03	-0.32			
P40121	Macrophage-capping protein	12	54	-0.60	-0.34	0.38	5		
Q8NDA8	Maestro heat-like repeat-containing protein family member 1	1	5	NA	NA	NA			
Q68CQ1	Maestro heat-like repeat-containing protein family member 7	1	2	NA	NA	NA			
Q9H0U3	Magnesium transporter protein 1	2	2	0.72	0.49	-0.24			
Q86V88	Magnesium-dependent phosphatase 1	3	3	-0.39	-0.67	-0.27			
Q9NZW5	MAGUK p55 subfamily member 6	1	1	0.22	-0.60	-0.82			
Q5T2T1	MAGUK p55 subfamily member 7	2	3	0.33	-0.27	-0.59			
P07199	Major centromere autoantigen B	4	14	-0.17	0.10	0.26			
P04156	Major prion protein	1	10	1.04	0.96	-0.08			
Q14764	Major vault protein	36	208	-0.53	-0.37	0.12	5		
P40925	Malate dehydrogenase, cytoplasmic	17	207	0.27	-0.30	-0.63			5
P40926	Malate dehydrogenase, mitochondrial	29	689	0.07	-0.08	-0.04			
Q9BSQ5	Malcavernin	1	4	-0.31	0.08	0.52			
Q14165	Malectin	4	10	0.31	0.78	0.32		5	
Q68DK7	Male-specific lethal 1 homolog	6	17	-0.05	0.11	0.12			
O43708	Maleylacetoacetate isomerase	1	3	-0.09	-0.15	-0.12			
Q9ULC4	Malignant T-cell-amplified sequence 1	5	26	0.27	0.11	-0.15			
O95822	Malonyl-CoA decarboxylase, mitochondrial	4	9	-0.02	0.06	0.23			
Q8IVS2	Malonyl-CoA-acyl carrier protein transacylase, mitochondrial	1	1	-0.12	0.38	0.48			

Q9UM22	Mammalian ependymin-related protein 1	1	1	-2.85	-0.97	1.88			
Q961J6	Mannose-1-phosphate guanyltransferase alpha	7	26	0.26	0.42	0.34		5	
Q9Y5P6	Mannose-1-phosphate guanyltransferase beta	5	25	0.38	0.55	0.28		5	
P34949	Mannose-6-phosphate isomerase	7	25	0.42	-0.12	-0.49			
Q13724	Mannosyl-oligosaccharide glucosidase	11	40	0.34	0.17	0.10			
P49137	MAP kinase-activated protein kinase 2	8	24	0.04	0.40	0.53			
Q16644	MAP kinase-activated protein kinase 3	2	9	-0.43	0.05	0.48			
Q8WXG6	MAP kinase-activating death domain protein	2	4	-0.58	-0.06	0.53			
P27448	MAP/microtubule affinity-regulating kinase 3	7	10	-0.18	0.17	0.16			
Q3KQU3	MAP7 domain-containing protein 1	11	44	-0.26	-0.30	-0.08			
Q8IWC1	MAP7 domain-containing protein 3	1	1	0.20	0.25	0.05			
P49006	MARCKS-related protein	6	11	-0.99	-0.96	0.04	3	4	
Q92585	Mastermind-like protein 1	2	2	-0.43	0.25	0.68			
P43243	Matrin-3	24	164	-0.16	-0.20	-0.08			
P14780	Matrix metalloproteinase-9	1	2	0.53	-0.50	-1.02			
Q9NR99	Matrix-remodeling-associated protein 5	1	1	-0.57	-0.16	0.41			
P84157	Matrix-remodeling-associated protein 7	3	7	0.17	0.79	0.66		3	4
Q8IWT9	MAX gene-associated protein	1	1	NA	NA	NA			
Q99583	Max-binding protein MNT	1	1	-0.16	-0.27	-0.12			
Q96DY7	Mdm2-binding protein	1	1	-0.40	-0.26	0.14			
Q14676	Mediator of DNA damage checkpoint protein 1	11	39	-0.27	-0.15	0.12			
Q15648	Mediator of RNA polymerase II transcription subunit 1	6	14	-0.26	-0.12	0.23			
Q9BTT4	Mediator of RNA polymerase II transcription subunit 10	2	4	-0.08	-0.19	-0.22			
Q93074	Mediator of RNA polymerase II transcription subunit 12	4	7	-0.39	-0.27	0.11			
O60244	Mediator of RNA polymerase II transcription subunit 14	1	15	NA	NA	NA			
Q96RN5	Mediator of RNA polymerase II transcription subunit 15	2	4	0.00	0.11	0.12			
Q9Y2X0	Mediator of RNA polymerase II transcription subunit 16	1	1	-0.05	-0.06	-0.01			
Q9NVC6	Mediator of RNA polymerase II transcription subunit 17	3	5	-0.10	-0.03	0.00			
Q9H944	Mediator of RNA polymerase II transcription subunit 20	4	6	-0.38	-0.18	0.20			
Q13503	Mediator of RNA polymerase II transcription subunit 21	1	1	-0.44	-0.46	-0.04			
Q15528	Mediator of RNA polymerase II transcription subunit 22	2	11	-0.12	-0.11	0.05			
Q9ULK4	Mediator of RNA polymerase II transcription subunit 23	1	1	-0.17	-0.13	0.05			
Q71SYS	Mediator of RNA polymerase II transcription subunit 25	2	2	-0.16	-0.07	0.08			
Q9H204	Mediator of RNA polymerase II transcription subunit 28	1	1	-0.86	-0.62	0.26			
Q9NX70	Mediator of RNA polymerase II transcription subunit 29	2	3	0.10	0.01	-0.02			
Q9NPJ6	Mediator of RNA polymerase II transcription subunit 4	1	1	NA	NA	NA			
O75586	Mediator of RNA polymerase II transcription subunit 6	2	2	-1.99	-1.67	0.33			
O43513	Mediator of RNA polymerase II transcription subunit 7	1	1	-0.32	-0.32	0.00			
P11310	Medium-chain specific acyl-CoA dehydrogenase, mitochondrial	15	66	0.04	0.03	-0.02			
P42679	Megakaryocyte-associated tyrosine-protein kinase	5	21	-0.70	0.51	1.11	4	5	4
Q5JRA6	Melanoma inhibitory activity protein 3	8	21	0.19	0.09	0.10			
Q9UNF1	Melanoma-associated antigen D2	10	32	0.16	-0.33	-0.38			
Q96MG7	Melanoma-associated antigen G1	3	7	-0.26	-0.44	0.17			
P15529	Membrane cofactor protein	1	1	0.88	0.49	-0.38			
Q8N4V1	Membrane magnesium transporter 1	1	6	-0.13	-0.06	0.09			
Q5TCQ9	Membrane-associated guanylate kinase, WW and PDZ domain-containing p	1	1	NA	NA	NA			
O00562	Membrane-associated phosphatidylinositol transfer protein 1	7	12	0.39	0.17	-0.13			
O00264	Membrane-associated progesterone receptor component 1	1	2	-0.02	0.05	0.07			
O15173	Membrane-associated progesterone receptor component 2	4	16	-0.03	0.03	0.07			
O00255	Menin	6	18	0.12	-0.06	-0.18			
P35240	Merlin	3	7	-0.40	0.61	0.83			4
P55145	Mesencephalic astrocyte-derived neurotrophic factor	6	20	-0.12	0.18	0.37			
Q8N108	Mesoderm induction early response protein 1	3	8	0.42	0.22	-0.19			
Q68D91	Metallo-beta-lactamase domain-containing protein 2	2	3	-0.01	-0.13	-0.13			
Q96E52	Metalloendopeptidase OMA1, mitochondrial	1	21	-0.40	-0.66	-0.25			
P04732	Metallothionein-1E	1	1	0.14	-0.81	-0.97			
P02795	Metallothionein-2	1	9	0.24	-0.36	-0.60			
O43312	Metastasis suppressor protein 1	6	13	-1.49	-0.05	1.56	3		3
Q13330	Metastasis-associated protein MTA1	4	22	0.08	-0.26	-0.44			
O94776	Metastasis-associated protein MTA2	21	94	-0.16	0.11	0.26			
Q13505	Metaxin-1	2	9	0.12	-0.03	-0.12			
O75431	Metaxin-2	1	6	0.25	-0.04	-0.21			
Q2M296	Methylenetetrahydrofolate synthase domain-containing protein	1	1	-0.20	0.04	0.23			
Q9NZL9	Methionine adenosyltransferase 2 subunit beta	9	53	-0.11	0.00	0.10			
P53582	Methionine aminopeptidase 1	5	15	0.38	0.33	-0.05			
P50579	Methionine aminopeptidase 2	9	47	0.36	-0.03	-0.37			
Q99707	Methionine synthase	1	1	0.41	0.16	-0.24			
P56192	Methionine--tRNA ligase, cytoplasmic	12	43	0.32	0.24	-0.15			
Q96GW9	Methionine--tRNA ligase, mitochondrial	1	1	NA	NA	NA			
Q96DP5	Methionyl-tRNA formyltransferase, mitochondrial	1	1	-0.10	-0.22	-0.11			
P16455	Methylated-DNA--protein-cysteine methyltransferase	7	32	-0.16	-0.25	-0.13			
Q9UI59	Methyl-CpG-binding domain protein 1	5	27	-0.15	-0.07	0.15			
Q9UBB5	Methyl-CpG-binding domain protein 2	8	27	-0.05	0.11	0.17			
O95983	Methyl-CpG-binding domain protein 3	3	4	-0.42	-0.27	0.14			
O95243	Methyl-CpG-binding domain protein 4	1	5	-0.03	-0.04	0.00			
P51608	Methyl-CpG-binding protein 2	29	329	0.53	0.07	-0.38	4		
Q9HCC0	Methylcrotonoyl-CoA carboxylase beta chain, mitochondrial	11	38	0.30	-0.24	-0.38			
Q96RQ3	Methylcrotonoyl-CoA carboxylase subunit alpha, mitochondrial	11	38	0.12	-0.16	-0.33			
P42898	Methylenetetrahydrofolate reductase	1	5	-0.45	-0.09	0.37			
Q13825	Methylglutaconyl-CoA hydratase, mitochondrial	7	17	0.12	0.12	-0.09			
Q02252	Methylmalonate-semialdehyde dehydrogenase, mitochondrial	14	51	0.68	0.00	-0.67	5		4
Q8IVH4	Methylmalonic aciduria type A protein, mitochondrial	4	9	0.10	-0.16	-0.18			
Q96PE7	Methylmalonyl-CoA epimerase, mitochondrial	5	14	0.19	0.10	-0.14			
P22033	Methylmalonyl-CoA mutase, mitochondrial	12	31	0.10	-0.11	-0.17			
Q9BQA1	Methylosome protein 50	2	15	0.34	0.07	-0.30			
P54105	Methylosome subunit pICln	4	14	0.19	-0.31	-0.42			

Q9BV20	Methylthioribose-1-phosphate isomerase	7	30	0.22	0.23	0.04		
Q96GX9	Methylthioribulose-1-phosphate dehydratase	4	14	0.27	0.07	-0.16		
Q8N6R0	Methyltransferase-like protein 13	4	7	0.09	-0.06	-0.18		
Q9HCE5	Methyltransferase-like protein 14	2	6	-0.08	-0.15	-0.14		
Q86W50	Methyltransferase-like protein 16	3	8	0.07	-0.16	-0.20		
Q9H8H3	Methyltransferase-like protein 7A	2	3	-1.09	-0.01	1.09		
P22670	MHC class II regulatory factor RFX1	8	18	0.01	-0.06	0.02		
Q8N3F8	MICAL-like protein 1	1	1	-0.22	0.17	0.39		
P55082	Microfibril-associated glycoprotein 3	1	1	NA	NA	NA		
P55081	Microfibrillar-associated protein 1	7	31	-0.19	-0.15	0.07		
Q99735	Microsomal glutathione S-transferase 2	1	1	-0.72	0.22	0.94		
O14880	Microsomal glutathione S-transferase 3	1	2	-0.36	-0.28	0.09		
Q9UPN3	Microtubule-actin cross-linking factor 1, isoforms 1/2/3/5	39	102	-0.06	0.08	0.13		
Q66K74	Microtubule-associated protein 1S	11	37	0.07	0.18	0.07		
P27816	Microtubule-associated protein 4	37	199	-0.26	0.22	0.57		
Q15691	Microtubule-associated protein RP/EB family member 1	10	67	-0.03	0.16	0.13		
Q15555	Microtubule-associated protein RP/EB family member 2	8	23	-0.29	-0.02	0.36		
O60307	Microtubule-associated serine/threonine-protein kinase 3	2	10	-0.25	-0.03	0.41		
O15021	Microtubule-associated serine/threonine-protein kinase 4	1	7	0.82	-0.08	-0.90		
Q9NUJ2	Midasin	1	1	NA	NA	NA		
A9UHW6	MIF4G domain-containing protein	1	2	-0.36	0.15	0.50		
Q8N183	Mimitin, mitochondrial	4	9	0.30	0.00	-0.18		
Q9BTE3	Mini-chromosome maintenance complex-binding protein	4	13	0.20	0.33	-0.01		
Q92619	Minor histocompatibility protein HA-1	31	214	0.06	-0.13	-0.17		
Q9H5X1	MIP18 family protein FAM96A	2	5	0.23	0.12	-0.11		
P54278	Mismatch repair endonuclease PMS2	1	1	-0.44	-0.25	0.17		
Q8N4C8	Misshapen-like kinase 1	3	19	0.57	0.31	-0.30		
Q02978	Mitochondrial 2-oxoglutarate/malate carrier protein	5	31	0.02	0.13	0.22		
Q7Z434	Mitochondrial antiviral-signaling protein	7	22	0.29	0.30	0.04		
O43772	Mitochondrial carnitine/acylcarnitine carrier protein	1	2	NA	NA	NA		
Q9NZJ7	Mitochondrial carrier homolog 1	1	2	-0.49	-0.31	0.19		
Q9Y6C9	Mitochondrial carrier homolog 2	4	21	-0.11	0.15	0.17		
Q86VD7	Mitochondrial coenzyme A transporter SLC25A42	1	3	-0.41	-0.07	0.34		
Q9UBX3	Mitochondrial dicarboxylate carrier	1	1	NA	NA	NA		
Q9NQG6	Mitochondrial dynamics protein MID51	2	7	-0.08	-0.01	0.03		
Q7L5Y1	Mitochondrial enolase superfamily member 1	1	1	NA	NA	NA		
Q9Y3D6	Mitochondrial fission 1 protein	3	10	0.38	0.08	-0.26		
Q9GZY8	Mitochondrial fission factor	3	12	-0.01	0.24	0.23		
Q9UDX5	Mitochondrial fission process protein 1	1	4	0.44	0.04	-0.40		
Q9H019	Mitochondrial fission regulator 1-like	2	5	0.19	-0.13	-0.35		
Q9BQP7	Mitochondrial genome maintenance exonuclease 1	1	1	-0.16	-0.13	0.01		
Q9H936	Mitochondrial glutamate carrier 1	8	29	-0.06	0.05	0.18		
P62072	Mitochondrial import inner membrane translocase subunit Tim10	3	10	0.20	0.00	-0.24		
Q9Y5J6	Mitochondrial import inner membrane translocase subunit Tim10 B	1	1	1.60	1.27	-0.32		
Q9Y5L4	Mitochondrial import inner membrane translocase subunit Tim13	2	26	-0.09	0.00	0.01		
Q96DA6	Mitochondrial import inner membrane translocase subunit TIM14	2	6	-0.15	-0.11	0.09		
Q9Y3D7	Mitochondrial import inner membrane translocase subunit TIM16	3	9	0.20	-0.19	-0.15		
Q9BVV7	Mitochondrial import inner membrane translocase subunit Tim21	1	1	-0.02	0.08	0.10		
O43615	Mitochondrial import inner membrane translocase subunit TIM44	11	29	0.09	0.03	-0.08		
Q32CQ8	Mitochondrial import inner membrane translocase subunit TIM50	7	18	0.08	0.04	0.03		
O60220	Mitochondrial import inner membrane translocase subunit Tim8 A	1	7	0.43	-0.26	-0.49		
Q9Y5J7	Mitochondrial import inner membrane translocase subunit Tim9	4	17	0.26	-0.20	-0.42		
Q15388	Mitochondrial import receptor subunit TOM20 homolog	2	9	0.05	0.06	0.16		
Q9NS69	Mitochondrial import receptor subunit TOM22 homolog	4	25	0.18	0.01	-0.17		
Q15785	Mitochondrial import receptor subunit TOM34	3	12	-0.36	-0.17	0.21		
O96008	Mitochondrial import receptor subunit TOM40 homolog	4	6	0.22	0.06	-0.16		
Q969M1	Mitochondrial import receptor subunit TOM40B	1	1	0.01	0.01	0.00		
Q8N4H5	Mitochondrial import receptor subunit TOM5 homolog	2	8	0.35	-0.24	-0.29		
Q96B49	Mitochondrial import receptor subunit TOM6 homolog	1	7	-0.26	0.10	0.19		
O94826	Mitochondrial import receptor subunit TOM70	11	41	0.01	-0.10	-0.16		
Q16891	Mitochondrial inner membrane protein	38	235	0.15	0.07	-0.17		
Q15070	Mitochondrial inner membrane protein OXA1L	2	7	0.14	0.11	-0.03		
Q99797	Mitochondrial intermediate peptidase	1	2	0.63	0.26	-0.36		
Q8N4Q1	Mitochondrial intermembrane space import and assembly protein 40	1	1	-0.89	-0.79	0.11		
Q9UJ68	Mitochondrial peptide methionine sulfoxide reductase	5	10	0.07	-0.23	-0.33		
Q8IXI2	Mitochondrial Rho GTPase 1	1	2	-0.19	-0.11	0.09		
Q8IXI1	Mitochondrial Rho GTPase 2	4	14	-0.06	0.12	0.08		
Q7L0Y3	Mitochondrial ribonuclease P protein 1	10	19	0.58	0.12	-0.64	4	4
Q86UD5	Mitochondrial sodium/hydrogen exchanger 9B2	1	3	0.59	1.11	0.52		
Q9HC21	Mitochondrial thiamine pyrophosphate carrier	2	3	-0.14	0.06	0.21		
Q96BW9	Mitochondrial translocator assembly and maintenance protein 41 homolog	2	2	0.05	-0.18	-0.23		
Q10713	Mitochondrial-processing peptidase subunit alpha	5	17	0.10	0.16	-0.08		
O75439	Mitochondrial-processing peptidase subunit beta	11	45	0.10	0.01	-0.06		
Q8IWA4	Mitofusin-1	1	2	NA	NA	NA		
O95140	Mitofusin-2	2	3	0.04	0.03	-0.02		
P28482	Mitogen-activated protein kinase 1	9	112	-0.02	0.46	0.53	5	
O15264	Mitogen-activated protein kinase 13	4	21	0.14	-0.14	-0.37		
Q16539	Mitogen-activated protein kinase 14	7	18	-0.11	0.33	0.43		
P27361	Mitogen-activated protein kinase 3	5	29	0.28	0.18	-0.23		
Q13164	Mitogen-activated protein kinase 7	2	2	0.05	0.44	0.39		
P45983	Mitogen-activated protein kinase 8	1	1	0.33	0.20	-0.14		
Q9Y2U5	Mitogen-activated protein kinase kinase kinase 2	2	2	0.30	0.32	0.02		
Q99759	Mitogen-activated protein kinase kinase kinase 3	2	2	0.19	0.31	0.12		
Q9Y6R4	Mitogen-activated protein kinase kinase kinase 4	1	2	0.57	0.48	-0.09		
Q99683	Mitogen-activated protein kinase kinase kinase 5	1	2	NA	NA	NA		
O43318	Mitogen-activated protein kinase kinase kinase 7	3	10	-0.19	-0.22	-0.03		

Q92918	Mitogen-activated protein kinase kinase kinase kinase 1	9	18	0.44	0.08	-0.38	5		
Q12851	Mitogen-activated protein kinase kinase kinase kinase 2	6	14	0.37	-0.49	-0.66		5	5
Q95819	Mitogen-activated protein kinase kinase kinase kinase 4	2	13	-0.01	-0.16	-0.15			
Q9Y4K4	Mitogen-activated protein kinase kinase kinase kinase 5	1	2	-0.13	0.39	0.51			
O43684	Mitotic checkpoint protein BUB3	14	92	-0.05	-0.07	-0.07			
Q9Y6D9	Mitotic spindle assembly checkpoint protein MAD1	9	19	-0.10	-0.04	0.18			
Q9Y3D0	Mitotic spindle-associated MXM complex subunit MIP18	3	17	0.06	0.26	0.18			
Q6NZ67	Mitotic-spindle organizing protein 2B	3	6	-0.23	-0.07	-0.14			
Q8NB16	Mixed lineage kinase domain-like protein	3	3	-0.23	0.06	0.53			
Q9BYG3	MKI67 FHA domain-interacting nucleolar phosphoprotein	5	11	0.25	-0.36	-0.58			
Q969V6	MKL/myocardin-like protein 1	3	8	-0.01	-0.17	0.01			
Q96T76	MMS19 nucleotide excision repair protein homolog	1	9	-0.43	0.09	0.52			
Q7L9L4	MOB kinase activator 1B	6	27	-0.18	0.05	0.25			
Q96BX8	MOB kinase activator 3A	4	22	-0.29	0.09	0.40			
P26038	Moesin	45	1368	-0.54	0.16	0.90	5		5
Q8N2K0	Monoacylglycerol lipase ABHD12	3	10	-0.89	0.11	0.85			
O60669	Monocarboxylate transporter 2	2	4	-1.75	-0.88	0.87			
P08571	Monocyte differentiation antigen CD14	2	2	0.82	0.21	-0.60			
Q6UB35	Monofunctional C1-tetrahydrofolate synthase, mitochondrial	1	1	0.37	0.35	-0.02			
Q99685	Monoglyceride lipase	1	1	-0.35	-0.63	-0.29			
Q9Y6X9	MORC family CW-type zinc finger protein 2	1	1	-0.17	0.45	0.60			
Q14149	MORC family CW-type zinc finger protein 3	6	8	-0.30	-0.25	0.16			
Q9Y605	MORF4 family-associated protein 1	1	8	0.03	0.10	0.00			
Q9UBU8	Mortality factor 4-like protein 1	6	24	0.08	-0.26	-0.33			
Q15014	Mortality factor 4-like protein 2	2	5	0.23	0.16	-0.11			
Q15796	Mothers against decapentaplegic homolog 2	1	13	-0.29	-0.11	0.18			
P84022	Mothers against decapentaplegic homolog 3	1	11	0.22	0.62	0.38			
Q13485	Mothers against decapentaplegic homolog 4	2	7	-0.08	-0.13	-0.04			
Q99547	M-phase phosphoprotein 6	2	3	0.11	-0.30	-0.49			
Q99549	M-phase phosphoprotein 8	3	13	-0.09	0.12	0.14			
Q8TAP9	M-phase-specific PLK1-interacting protein	1	5	0.02	-0.34	-0.36			
Q9NV56	MRG/MORF4L-binding protein	2	7	-0.02	-0.15	0.18			
O43148	mRNA cap guanine-N7 methyltransferase	10	36	0.06	-0.12	-0.20			
P78406	mRNA export factor	13	55	-0.06	-0.06	0.15			
Q9UKD2	mRNA turnover protein 4 homolog	4	11	0.35	-0.06	-0.44			
O60942	mRNA-capping enzyme	3	3	1.02	0.01	-1.01			
Q9NP16	mRNA-decapping enzyme 1A	7	25	-0.03	0.01	-0.04			
Q96T58	Msx2-interacting protein	12	21	-0.24	-0.16	0.06			
Q9H7C9	Mth938 domain-containing protein	3	11	-0.26	-0.36	0.05			
Q9UDY8	Mucosa-associated lymphoid tissue lymphoma translocation protein 1	3	5	0.19	0.20	0.00			
P08183	Multidrug resistance protein 1	9	16	0.55	1.07	0.42		4	
P22234	Multifunctional protein ADE2	15	51	0.15	-0.35	-0.43			
Q13201	Multimerin-1	7	9	0.01	-0.14	-0.22			
Q9BU76	Multiple myeloma tumor-associated protein 2	2	15	-0.06	0.13	0.21			
Q96EY5	Multivesicular body subunit 12A	4	8	-0.43	0.14	0.63			5
Q9NR56	Muscleblind-like protein 1	4	15	0.08	-0.12	-0.05			
Q9BQG0	Myb-binding protein 1A	13	37	0.33	-0.09	-0.22			
O00499	Myc box-dependent-interacting protein 1	16	109	-0.01	-0.15	-0.11			
P56270	Myc-associated zinc finger protein	3	3	-0.23	0.00	0.16			
Q8TB22	MYCBP-associated protein	1	2	-2.73	0.03	2.76			
Q9NUJ1	Mycophenolic acid acyl-glucuronide esterase, mitochondrial	9	36	0.49	0.19	-0.31			
P02686	Myelin basic protein	5	10	-1.16	0.12	1.40	4		4
Q9P2K5	Myelin expression factor 2	2	2	NA	NA	NA			
P41218	Myeloid cell nuclear differentiation antigen	8	30	-0.04	-0.15	-0.11			
Q99836	Myeloid differentiation primary response protein MyD88	3	7	-0.06	0.16	0.24			
Q15773	Myeloid leukemia factor 2	2	8	0.24	0.03	-0.20			
Q96S97	Myeloid-associated differentiation marker	1	5	-0.60	0.18	0.59			
P05164	Myeloperoxidase	12	40	0.21	-0.04	-0.11			
Q14814	Myocyte-specific enhancer factor 2D	3	4	-0.72	-0.06	0.66			
Q5VU43	Myomegalin	1	1	NA	NA	NA			
P14649	Myosin light chain 6B	1	168	-0.34	-0.15	0.20			
P60660	Myosin light polypeptide 6	9	318	0.00	0.08	0.05			
Q6WCQ1	Myosin phosphatase Rho-interacting protein	4	4	0.23	0.28	0.04			
P19105	Myosin regulatory light chain 12A	6	103	0.49	0.17	-0.22			
P24844	Myosin regulatory light polypeptide 9	1	46	-0.39	-0.27	0.12			
P35579	Myosin-9	173	3283	0.14	0.08	-0.11			
P58546	Myotrophin	3	36	-0.02	0.01	-0.01			
Q13496	Myotubularin	1	1	1.17	0.16	-1.01			
Q13613	Myotubularin-related protein 1	4	5	0.07	0.13	0.02			
Q9C0I1	Myotubularin-related protein 12	2	6	-0.33	-0.16	0.16			
Q8NCE2	Myotubularin-related protein 14	2	3	0.09	0.15	-0.10			
Q13615	Myotubularin-related protein 3	1	1	-0.43	0.36	0.80			
Q95248	Myotubularin-related protein 5	24	67	0.17	0.06	-0.02			
Q9Y217	Myotubularin-related protein 6	2	2	0.94	1.08	0.15			
P29966	Myristoylated alanine-rich C-kinase substrate	2	2	-0.25	-0.22	0.04			
P20933	N(4)-(beta-N-acetylglucosaminyl)-L-asparaginase	3	18	-0.33	0.68	1.06		3	5
O95865	N(G),N(G)-dimethylarginine dimethylaminohydrolase 2	10	56	-0.53	0.43	1.08		5	5
Q86U44	N6-adenosine-methyltransferase 70 kDa subunit	9	27	0.08	0.02	-0.14			
O14745	Na(+)/H(+) exchange regulatory cofactor NHE-RF1	22	190	-0.66	0.18	0.93	5		5
Q15599	Na(+)/H(+) exchange regulatory cofactor NHE-RF2	1	1	-1.70	-0.51	1.20			
Q9UJ70	N-acetyl-D-glucosamine kinase	10	46	0.11	0.13	0.13			
Q01415	N-acetylglactosamine kinase	3	4	0.14	0.23	0.10			
P34059	N-acetylglactosamine-6-sulfatase	2	2	-0.70	0.32	1.02			
P15586	N-acetylglucosamine-6-sulfatase	8	32	-0.59	0.81	1.42		5	5
O95671	N-acetylserotonin O-methyltransferase-like protein	7	25	-0.39	0.11	0.45			
Q9H0A0	N-acetyltransferase 10	18	66	0.43	0.02	-0.37			

Q93015	N-acetyltransferase 6	1	1	0.23	-0.24	-0.49			
Q5FWF5	N-acetyltransferase ESCO1	1	1	-1.20	-0.36	0.85			
Q56NI9	N-acetyltransferase ESCO2	1	4	NA	NA	NA			
Q9C000	NACHT, LRR and PYD domains-containing protein 1	4	6	0.06	-0.17	-0.18			
Q02083	N-acylethanolamine-hydrolyzing acid amidase	3	15	-0.07	-0.44	-0.29			
P51606	N-acylglucosamine 2-epimerase	2	12	-0.61	-0.40	0.21			
Q8NFW8	N-acylneuraminate cytidyltransferase	12	73	0.22	0.04	-0.27			
Q4G0N4	NAD kinase 2, mitochondrial	11	26	0.03	0.09	-0.02			
Q13423	NAD(P) transhydrogenase, mitochondrial	36	295	0.10	0.02	-0.01			
Q8NCW5	NAD(P)H-hydrate epimerase	7	28	-0.13	0.00	-0.01			
P23368	NAD-dependent malic enzyme, mitochondrial	12	66	-0.03	0.15	0.19			
Q96EB6	NAD-dependent protein deacetylase sirtuin-1	2	5	0.05	-0.24	-0.28			
Q8IXJ6	NAD-dependent protein deacetylase sirtuin-2	3	3	-0.28	0.32	0.60			
Q9NTG7	NAD-dependent protein deacetylase sirtuin-3, mitochondrial	1	3	0.66	-0.20	-0.86			
Q9NRC8	NAD-dependent protein deacetylase sirtuin-7	1	1	-0.12	0.08	0.21			
Q9NXA8	NAD-dependent protein deacetylase sirtuin-5, mitochondrial	3	4	0.04	0.11	0.20			
Q9BU61	NADH dehydrogenase 1 alpha subcomplex assembly factor 3	3	17	-0.11	-0.38	-0.27			
Q9P032	NADH dehydrogenase 1 alpha subcomplex assembly factor 4	4	5	-0.03	-0.50	-0.22			
O95299	NADH dehydrogenase 1 alpha subcomplex subunit 10, mitochondrial	10	38	0.32	-0.08	-0.35			
Q86Y39	NADH dehydrogenase 1 alpha subcomplex subunit 11	2	4	0.09	0.00	-0.15			
Q9UI09	NADH dehydrogenase 1 alpha subcomplex subunit 12	3	16	0.20	0.14	-0.02			
Q9P0J0	NADH dehydrogenase 1 alpha subcomplex subunit 13	4	7	0.32	-0.02	-0.30			
O43678	NADH dehydrogenase 1 alpha subcomplex subunit 2	7	35	0.04	0.08	-0.08			
O95167	NADH dehydrogenase 1 alpha subcomplex subunit 3	2	2	0.22	-0.41	-0.63			
O00483	NADH dehydrogenase 1 alpha subcomplex subunit 4	6	42	0.29	0.07	-0.10			
Q16718	NADH dehydrogenase 1 alpha subcomplex subunit 5	3	22	-0.06	-0.06	0.03			
P56556	NADH dehydrogenase 1 alpha subcomplex subunit 6	7	45	0.04	0.05	-0.05			
O95182	NADH dehydrogenase 1 alpha subcomplex subunit 7	9	50	0.05	-0.07	-0.09			
P51970	NADH dehydrogenase 1 alpha subcomplex subunit 8	4	11	0.10	-0.05	-0.23			
Q16795	NADH dehydrogenase 1 alpha subcomplex subunit 9, mitochondrial	6	21	0.36	0.20	-0.17			
O75438	NADH dehydrogenase 1 beta subcomplex subunit 1	2	4	0.38	-0.36	-0.74			
O96000	NADH dehydrogenase 1 beta subcomplex subunit 10	6	35	0.30	0.08	-0.12			
Q9NX14	NADH dehydrogenase 1 beta subcomplex subunit 11, mitochondrial	1	9	0.25	0.00	-0.16			
O43676	NADH dehydrogenase 1 beta subcomplex subunit 3	4	16	0.26	0.20	0.03			
O95168	NADH dehydrogenase 1 beta subcomplex subunit 4	3	29	0.37	-0.04	-0.32			
O43674	NADH dehydrogenase 1 beta subcomplex subunit 5, mitochondrial	2	11	0.31	0.03	-0.34			
O95139	NADH dehydrogenase 1 beta subcomplex subunit 6	2	2	-1.34	-1.21	0.14			
P17568	NADH dehydrogenase 1 beta subcomplex subunit 7	3	27	0.33	0.08	-0.20			
O95169	NADH dehydrogenase 1 beta subcomplex subunit 8, mitochondrial	3	10	0.29	0.20	-0.15			
Q9Y6M9	NADH dehydrogenase 1 beta subcomplex subunit 9	4	31	0.03	0.09	-0.06			
O95298	NADH dehydrogenase 1 subunit C2	2	5	0.08	-0.51	-0.58			
P49821	NADH dehydrogenase flavoprotein 1, mitochondrial	8	34	0.47	0.13	-0.32			
P19404	NADH dehydrogenase flavoprotein 2, mitochondrial	8	73	0.10	0.08	-0.06			
P56181	NADH dehydrogenase flavoprotein 3, mitochondrial	1	1	-0.59	0.25	0.85			
O75306	NADH dehydrogenase iron-sulfur protein 2, mitochondrial	9	19	0.34	-0.05	-0.22			
O75489	NADH dehydrogenase iron-sulfur protein 3, mitochondrial	9	62	0.38	-0.02	-0.30			
O43181	NADH dehydrogenase iron-sulfur protein 4, mitochondrial	3	5	0.03	-0.10	0.52			
O43920	NADH dehydrogenase iron-sulfur protein 5	2	4	0.05	0.00	-0.09			
O75380	NADH dehydrogenase iron-sulfur protein 6, mitochondrial	6	21	-0.17	-0.05	0.11			
O75251	NADH dehydrogenase iron-sulfur protein 7, mitochondrial	5	26	0.16	0.00	-0.20			
O00217	NADH dehydrogenase iron-sulfur protein 8, mitochondrial	6	14	0.10	0.00	-0.19			
Q9UHQ9	NADH-cytochrome b5 reductase 1	3	10	0.41	0.08	-0.47			
P00387	NADH-cytochrome b5 reductase 3	6	56	-0.09	0.36	0.24			
P28331	NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial	30	178	0.23	0.07	-0.20			
P03915	NADH-ubiquinone oxidoreductase chain 5	1	1	0.29	-0.13	-0.42			
P48163	NADP-dependent malic enzyme	3	4	2.86	1.97	-0.45	3		3
P22570	NADPH:adenodoxin oxidoreductase, mitochondrial	8	26	0.01	0.21	0.12			
P16435	NADPH--cytochrome P450 reductase	8	18	-0.26	0.01	0.29			
P41227	N-alpha-acetyltransferase 10	9	36	0.31	-0.17	-0.48			
Q9BXJ9	N-alpha-acetyltransferase 15, NatA auxiliary subunit	7	25	0.50	0.19	-0.24			
Q6N069	N-alpha-acetyltransferase 16, NatA auxiliary subunit	1	7	0.00	-0.71	-0.71			
Q147X3	N-alpha-acetyltransferase 30	2	6	0.01	0.08	0.09			
Q5VZE5	N-alpha-acetyltransferase 35, NatC auxiliary subunit	3	4	0.04	0.29	0.25			
O95777	N-alpha-acetyltransferase 38, NatC auxiliary subunit	5	42	0.02	-0.13	-0.19			
Q86UY6	N-alpha-acetyltransferase 40	2	2	-0.47	-0.09	0.37			
Q9GZZ1	N-alpha-acetyltransferase 50	5	8	0.21	0.19	-0.22			
O43847	Nardilysin	3	4	0.38	-0.07	-0.44			
Q13765	Nascent polypeptide-associated complex subunit alpha	6	76	0.28	0.07	-0.43			
Q9BZW8	Natural killer cell receptor 2B4	1	1	-0.51	0.51	1.03			
P55160	Nck-associated protein 1-like	9	33	0.08	0.36	0.24			
Q9HCH0	Nck-associated protein 5-like	1	1	-0.57	-0.89	-0.32			
O75113	NEDD4-binding protein 1	2	9	0.12	0.21	0.12			
O15049	NEDD4-binding protein 3	2	2	-0.34	-0.13	0.22			
Q9H0M0	NEDD4-like E3 ubiquitin-protein ligase WWP1	1	1	0.30	-0.05	-0.35			
O00308	NEDD4-like E3 ubiquitin-protein ligase WWP2	1	4	-0.04	0.02	0.06			
Q15843	NEDD8	6	22	-0.19	-0.15	0.01			
Q9Y5A7	NEDD8 ultimate buster 1	8	15	-0.20	-0.07	0.07			
Q8TBC4	NEDD8-activating enzyme E1 catalytic subunit	9	26	-0.21	-0.03	0.04			
Q13564	NEDD8-activating enzyme E1 regulatory subunit	6	33	-0.14	-0.01	0.03			
P61081	NEDD8-conjugating enzyme Ubc12	6	26	-0.15	0.13	0.17			
Q969M7	NEDD8-conjugating enzyme UBE2F	1	4	-0.29	0.13	0.42			
Q9H3P2	Negative elongation factor A	10	34	-0.08	0.05	0.01			
Q8WX92	Negative elongation factor B	2	2	0.04	-0.04	-0.07			
Q8IXH7	Negative elongation factor C/D	4	5	0.42	0.27	0.18			
P18615	Negative elongation factor E	13	53	-0.14	-0.11	0.01			
Q8NPF1	Nesprin-1	45	99	0.07	0.24	0.30			

Q8WXH0	Nesprin-2	60	138	0.40	0.61	0.25		5	
Q6ZMZ3	Nesprin-3	4	14	-0.24	-0.03	-0.03			
Q9UMX5	Neudesin	1	1	-0.01	-0.33	-0.31			
Q96SB3	Neurabin-2	16	49	-0.29	0.11	0.45			5
P13591	Neural cell adhesion molecule 1	3	6	-0.51	0.44	1.51			3
Q6ZNJ1	Neurobeachin-like protein 2	10	14	-0.41	0.66	0.60			
Q09666	Neuroblast differentiation-associated protein AHNAK	302	2300	0.49	0.99	0.56		3	4
A2RRP1	Neuroblastoma-amplified sequence	2	6	0.14	-0.11	-0.55			
P61601	Neurocalcin-delta	1	15	0.04	0.46	0.43			
Q9UBB6	Neurochondrin	1	5	1.04	0.97	-0.07			
Q04721	Neurogenic locus notch homolog protein 2	1	1	-1.49	-0.26	1.25			
Q9UM47	Neurogenic locus notch homolog protein 3	1	3	-0.02	0.11	0.09			
Q92686	Neurogranin	2	3	-0.48	0.02	0.51			
Q8NEJ9	Neuroguidin	4	8	0.34	-0.17	-0.52			
Q8IY17	Neuropathy target esterase	6	18	0.24	0.24	0.04			
Q9Y639	Neuroplastin	3	7	0.03	0.42	0.45			
Q14697	Neutral alpha-glucosidase AB	30	194	-0.29	0.07	0.30			
Q15758	Neutral amino acid transporter B(0)	1	2	0.14	0.27	0.14			
Q6PIU2	Neutral cholesterol ester hydrolase 1	3	15	-0.41	0.20	0.17			
P59665	Neutrophil defensin 1	1	3	NA	NA	NA			
P08246	Neutrophil elastase	1	1	0.50	0.12	-0.37			
Q0ZGT2	Nexilin	1	1	0.34	-0.40	-0.76			
Q8NCF5	NFATC2-interacting protein	4	20	-0.30	0.02	0.32			
Q9Y6K9	NF-kappa-B essential modulator	12	41	-0.33	-0.15	0.11			
P25963	NF-kappa-B inhibitor alpha	2	2	-0.33	-0.36	-0.03			
O00221	NF-kappa-B inhibitor epsilon	1	3	-0.58	-0.01	0.58			
Q9NYR9	NF-kappa-B inhibitor-interacting Ras-like protein 2	1	4	0.02	0.08	0.06			
Q8N5F7	NF-kappa-B-activating protein	2	2	-0.09	-0.34	-0.24			
O15226	NF-kappa-B-repressing factor	3	6	0.10	-0.05	-0.10			
Q6ZNB6	NF-X1-type zinc finger protein NFXL1	1	2	-0.19	0.25	0.43			
Q9P2E3	NFX1-type zinc finger-containing protein 1	2	4	-0.05	-0.20	0.17			
Q8NBF2	NHL repeat-containing protein 2	2	2	-0.29	0.42	0.71			
Q5JS37	NHL repeat-containing protein 3	2	2	-0.62	0.06	0.67			
P55769	NHP2-like protein 1	7	75	0.41	-0.12	-0.45			
Q5HYW2	NHS-like protein 2	7	13	0.10	0.75	0.94		3	3
Q96TA1	Niban-like protein 1	2	6	0.89	0.38	-0.57	3		
O60934	Nibrin	11	29	-0.40	-0.03	0.42			
Q969V3	Nicalin	5	17	0.12	0.26	0.27			
Q92542	Nicastrin	3	5	0.48	0.51	0.04			
Q9HAN9	Nicotinamide mononucleotide adenylyltransferase 1	6	9	-0.36	-0.01	0.26			
Q96T66	Nicotinamide mononucleotide adenylyltransferase 3	1	1	-0.17	-1.12	-0.94			
P43490	Nicotinamide phosphoribosyltransferase	14	62	0.27	0.13	-0.29			
Q9NWW6	Nicotinamide riboside kinase 1	1	5	0.24	0.22	0.07			
Q6XQN6	Nicotinate phosphoribosyltransferase	7	27	0.21	-0.10	-0.41			
O15118	Niemann-Pick C1 protein	1	1	-0.08	1.24	1.33			
Q8N4C6	Ninein	5	6	-0.15	-0.36	-0.17			
Q9Y2I6	Ninein-like protein	1	1	-0.01	0.17	0.18			
Q6KC79	Nipped-B-like protein	20	37	-0.19	-0.15	0.02			
Q9Y2I1	Nischarin	4	5	-0.25	-0.24	0.01			
Q9Y314	Nitric oxide synthase-interacting protein	7	23	-0.08	-0.90	-0.76		5	4
Q86X76	Nitrilase homolog 1	2	4	0.48	-0.14	-0.60			
Q12980	Nitrogen permease regulator 3-like protein	1	1	0.30	-0.28	-0.57			
P30414	NK-tumor recognition protein	3	3	0.31	0.04	-0.25			
Q86UT6	NLR family member X1	2	4	-0.64	-0.32	0.23			
Q659A1	NMDA receptor-regulated protein 2	1	2	0.02	-0.12	-0.15			
Q9HBL8	NmrA-like family domain-containing protein 1	3	6	-0.11	-0.10	-0.08			
Q13287	N-myc-interactor	5	8	0.12	-0.13	-0.20			
Q15155	Nodal modulator 1	1	32	-0.16	0.08	0.25			
P69849	Nodal modulator 3	1	32	-0.12	-0.19	-0.07			
P05114	Non-histone chromosomal protein HMG-14	7	42	0.38	-0.51	-1.05		4	3
P05204	Non-histone chromosomal protein HMG-17	3	27	-0.08	-1.13	-0.43		4	
Q15233	Non-POU domain-containing octamer-binding protein	20	425	-0.20	-0.19	0.05			
P29597	Non-receptor tyrosine-protein kinase TYK2	2	12	0.07	0.63	0.56			
P22307	Non-specific lipid-transfer protein	10	56	-0.78	-0.04	0.69	5		3
Q8WV22	Non-structural maintenance of chromosomes element 1 homolog	1	1	NA	NA	NA			
Q9NVX2	Notchless protein homolog 1	2	2	-0.04	-0.39	-0.35			
Q9UNZ2	NSFL1 cofactor p47	18	107	0.08	-0.17	-0.24			
P51688	N-sulphoglucosamine sulphohydrolase	5	30	0.32	-0.10	-0.45			
Q96KG9	N-terminal kinase-like protein	3	4	0.04	-0.19	-0.22			
Q9BV86	N-terminal Xaa-Pro-Lys N-methyltransferase 1	1	1	0.13	-0.18	-0.33			
P23497	Nuclear autoantigen Sp-100	8	38	-0.08	0.00	-0.01			
P49321	Nuclear autoantigenic sperm protein	11	96	-0.10	-0.16	-0.09			
Q13342	Nuclear body protein SP140	1	2	0.18	0.24	0.07			
Q9H930	Nuclear body protein SP140-like protein	1	3	0.59	0.19	-0.39			
Q09161	Nuclear cap-binding protein subunit 1	5	11	-0.23	-0.20	-0.02			
P52298	Nuclear cap-binding protein subunit 2	1	5	0.25	-0.05	-0.29			
Q9NXR1	Nuclear distribution protein nudE homolog 1	5	22	-0.36	-0.08	0.29			
Q9GZM8	Nuclear distribution protein nudE-like 1	1	10	-0.55	-0.27	0.30			
A8CG34	Nuclear envelope pore membrane protein POM 121C	7	16	-0.17	-0.03	0.10			
O60524	Nuclear export mediator factor NEMF	6	6	0.14	0.03	-0.11			
O00712	Nuclear factor 1 B-type	1	1	0.37	0.05	-0.33			
Q00653	Nuclear factor NF-kappa-B p100 subunit	18	57	0.37	0.03	-0.49			
P19838	Nuclear factor NF-kappa-B p105 subunit	26	157	0.23	-0.33	-0.50			
O95644	Nuclear factor of activated T-cells, cytoplasmic 1	2	11	0.52	-0.07	-0.59			
Q13469	Nuclear factor of activated T-cells, cytoplasmic 2	21	144	-0.74	0.19	0.89	5		5
Q12968	Nuclear factor of activated T-cells, cytoplasmic 3	3	19	-0.60	-0.16	0.31			

Q6P4R8	Nuclear factor related to kappa-B-binding protein	5	10	-0.01	0.01	-0.05			
Q9UHK0	Nuclear fragile X mental retardation-interacting protein 1	1	1	0.14	0.15	0.02			
Q7Z417	Nuclear fragile X mental retardation-interacting protein 2	4	8	-0.33	-0.07	0.24			
Q12972	Nuclear inhibitor of protein phosphatase 1	10	41	-0.23	-0.22	-0.09			
Q9Y266	Nuclear migration protein nudC	16	74	-0.06	-0.03	0.04			
Q14980	Nuclear mitotic apparatus protein 1	114	664	-0.37	-0.28	0.08			
Q13901	Nuclear nucleic acid-binding protein C1D	1	1	0.53	0.20	-0.33			
P57740	Nuclear pore complex protein Nup107	5	18	-0.28	0.03	0.29			
Q8WUM0	Nuclear pore complex protein Nup133	11	36	-0.02	0.13	0.25			
P49790	Nuclear pore complex protein Nup153	29	91	-0.26	0.03	0.36			
O75694	Nuclear pore complex protein Nup155	11	34	-0.16	0.07	0.31			
Q12769	Nuclear pore complex protein Nup160	1	4	0.04	0.12	0.13			
Q92621	Nuclear pore complex protein Nup205	9	27	0.06	0.14	0.12			
P35658	Nuclear pore complex protein Nup214	26	96	-0.06	0.04	0.10			
Q9UKX7	Nuclear pore complex protein Nup50	13	49	-0.21	-0.18	-0.04			
Q9BW27	Nuclear pore complex protein Nup85	5	8	-0.05	0.08	0.13			
Q99567	Nuclear pore complex protein Nup88	11	32	-0.08	-0.06	0.06			
Q8N1F7	Nuclear pore complex protein Nup93	14	71	-0.23	0.04	0.26			
P52948	Nuclear pore complex protein Nup98-Nup96	13	49	-0.14	0.11	0.22			
P37198	Nuclear pore glycoprotein p62	6	9	-0.10	0.10	0.14			
Q8TEM1	Nuclear pore membrane glycoprotein 210	26	88	0.01	0.27	0.24			
Q8TAT6	Nuclear protein localization protein 4 homolog	6	11	-0.01	0.04	0.01			
Q8TC05	Nuclear protein MDM1	4	7	-0.33	-0.23	0.13			
Q86WQ0	Nuclear receptor 2C2-associated protein	3	5	0.35	-0.16	-0.36			
Q15788	Nuclear receptor coactivator 1	1	2	-0.85	-0.62	0.21			
Q15596	Nuclear receptor coactivator 2	5	8	-0.02	0.11	0.00			
Q9Y6Q9	Nuclear receptor coactivator 3	3	5	-0.88	-0.48	0.26			
Q9HCD5	Nuclear receptor coactivator 5	9	45	-0.06	0.01	0.15			
Q14686	Nuclear receptor coactivator 6	4	8	-0.19	0.09	0.11			
Q8NI08	Nuclear receptor coactivator 7	1	1	NA	NA	NA			
O75376	Nuclear receptor corepressor 1	23	64	-0.14	-0.18	-0.07			
Q9Y618	Nuclear receptor corepressor 2	5	10	-0.65	-0.10	0.07			
P49116	Nuclear receptor subfamily 2 group C member 2	9	30	-0.15	-0.12	0.00			
Q9UHY1	Nuclear receptor-binding protein	6	17	0.16	0.09	-0.04			
Q16656	Nuclear respiratory factor 1	4	16	-0.18	-0.06	0.06			
Q9UBU9	Nuclear RNA export factor 1	8	34	-0.15	-0.12	0.02			
Q9H0G5	Nuclear speckle splicing regulatory protein 1	3	6	-0.18	-0.23	-0.04			
P23511	Nuclear transcription factor Y subunit alpha	2	34	-0.21	-0.16	0.02			
P25208	Nuclear transcription factor Y subunit beta	1	1	-1.12	-0.31	0.83			
Q13952	Nuclear transcription factor Y subunit gamma	4	16	0.11	0.02	-0.03			
P61970	Nuclear transport factor 2	4	49	0.39	-0.07	-0.25			
Q9H1E3	Nuclear ubiquitous casein and cyclin-dependent kinase substrate 1	9	74	-0.17	-0.28	-0.06			
O15381	Nuclear valosin-containing protein-like	1	5	NA	NA	NA			
Q86WB0	Nuclear-interacting partner of ALK	5	13	-0.37	-0.16	0.11			
Q9Y2C4	Nuclease EXOG, mitochondrial	2	6	0.08	-0.19	-0.11			
P67809	Nuclease-sensitive element-binding protein 1	5	70	0.17	0.14	0.09			
Q02818	Nucleobindin-1	8	27	-0.41	0.44	0.65			5
P80303	Nucleobindin-2	5	9	-0.01	-0.19	-0.16			
Q14978	Nucleolar and coiled-body phosphoprotein 1	16	73	0.53	0.10	-0.45			
Q9Y3T9	Nucleolar complex protein 2 homolog	2	5	0.51	-0.31	-0.81			
Q8WTT2	Nucleolar complex protein 3 homolog	3	8	0.34	-0.25	-0.51			
Q9BV14	Nucleolar complex protein 4 homolog	1	1	0.50	-0.05	-0.54			
Q9BZE4	Nucleolar GTP-binding protein 1	11	32	0.19	-0.09	-0.29			
Q13823	Nucleolar GTP-binding protein 2	3	7	-0.06	-0.17	-0.01			
Q5C9Z4	Nucleolar MIF4G domain-containing protein 1	5	14	0.27	-0.15	-0.35			
Q9BSC4	Nucleolar protein 10	2	6	0.58	-0.11	-0.64			3
Q9H8H0	Nucleolar protein 11	2	6	0.40	-0.02	-0.33			
Q9UGY1	Nucleolar protein 12	1	1	-1.04	-0.65	0.41			
P78316	Nucleolar protein 14	6	11	0.30	-0.23	-0.53			
Q9Y3C1	Nucleolar protein 16	3	13	0.33	-0.19	-0.10			
O00567	Nucleolar protein 56	33	217	0.57	0.05	-0.55	5		5
Q9Y2X3	Nucleolar protein 58	20	204	0.62	0.06	-0.65	5		5
Q9H6R4	Nucleolar protein 6	7	17	0.31	-0.09	-0.75			3
Q9UMY1	Nucleolar protein 7	4	22	0.02	-0.15	-0.37			
Q76FK4	Nucleolar protein 8	2	10	0.87	-0.17	-0.89	3		3
Q86U38	Nucleolar protein 9	5	9	0.28	0.01	-0.21			
Q9NP64	Nucleolar protein of 40 kDa	1	2	-0.58	-0.48	0.11			
Q9NR30	Nucleolar RNA helicase 2	20	85	0.49	-0.13	-0.62	5		5
P17480	Nucleolar transcription factor 1	19	73	0.32	-0.06	-0.26			
P19338	Nucleolin	54	671	0.13	-0.19	-0.20			
P31483	Nucleolysin TIA-1 isoform p40	2	30	-0.38	-0.48	0.06			
Q01085	Nucleolysin TIAR	5	35	0.01	-0.07	-0.09			
P06748	Nucleophosmin	14	369	0.44	-0.14	-0.49			
Q53GS7	Nucleoporin GLE1	4	7	0.03	0.05	-0.03			
Q9BTX1	Nucleoporin NDC1	2	4	-0.02	0.04	0.06			
Q5SRE5	Nucleoporin NUP188 homolog	1	1	-0.26	-0.22	0.04			
Q8NFH4	Nucleoporin Nup37	3	3	-0.08	0.02	0.29			
Q8NFH3	Nucleoporin Nup43	3	12	-0.31	-0.14	0.15			
Q8NFH5	Nucleoporin NUP53	7	60	-0.18	0.04	0.20			
Q7Z3B4	Nucleoporin p54	7	17	-0.01	0.14	0.08			
Q9BVL2	Nucleoporin p58/p45	4	6	-0.47	0.00	0.48			
Q96EE3	Nucleoporin SEH1	6	23	0.01	-0.11	-0.18			
P12270	Nucleoprotein TPR	85	321	-0.23	-0.04	0.17			
Q13232	Nucleoside diphosphate kinase 3	2	9	-0.52	-0.13	0.44			
O75414	Nucleoside diphosphate kinase 6	1	2	-0.55	0.10	0.65			
Q9Y5B8	Nucleoside diphosphate kinase 7	1	3	-0.29	-0.50	-0.22			

P15531	Nucleoside diphosphate kinase A	1	70	-1.32	-1.77	-0.44			
P22392	Nucleoside diphosphate kinase B	7	94	0.35	0.14	-0.19			
A8MXV4	Nucleoside diphosphate-linked moiety X motif 19, mitochondrial	2	3	0.25	0.13	-0.08			
P55209	Nucleosome assembly protein 1-like 1	5	67	0.21	-0.24	-0.48			
Q99733	Nucleosome assembly protein 1-like 4	13	116	0.03	-0.75	-0.84		5	5
Q12830	Nucleosome-remodeling factor subunit BPTF	8	20	-0.11	0.01	0.13			
Q96RE7	Nucleus accumbens-associated protein 1	2	3	-0.17	0.73	0.89			
Q96RS6	NudC domain-containing protein 1	3	9	0.06	-0.09	-0.15			
Q8WVJ2	NudC domain-containing protein 2	4	12	0.01	-0.14	-0.21			
Q8IVD9	NudC domain-containing protein 3	2	5	-0.09	-0.24	-0.22			
Q86Y26	NUT family member 1	1	1	0.01	0.31	0.31			
Q9Y530	O-acetyl-ADP-ribose deacetylase 1	4	5	0.01	-0.40	-0.45			
Q9BQ69	O-acetyl-ADP-ribose deacetylase MACROD1	2	4	0.29	0.13	-0.12			
Q9NTK5	Obg-like ATPase 1	8	54	-0.09	0.04	0.07			
Q9NX40	OCIA domain-containing protein 1	6	25	0.24	0.12	0.01			
Q56VL3	OCIA domain-containing protein 2	1	2	0.23	-0.49	-0.72			
Q8NGR8	Olfactory receptor 1L8	1	3	0.42	0.48	0.06			
Q9Y3B8	Oligoribonuclease, mitochondrial	3	13	0.32	0.36	-0.84			3
Q9NQR4	Omega-amidase NIT2	12	55	0.11	-0.07	-0.40			
Q9HD40	O-phosphoseryl-tRNA(Sec) selenium transferase	2	6	NA	NA	NA			
Q9NZT2	Opioid growth factor receptor	17	86	-0.05	-0.07	0.01			
Q9H6K4	Optic atrophy 3 protein	1	2	0.08	-0.08	-0.17			
Q96CV9	Optineurin	15	68	-0.19	0.20	0.38			
Q13416	Origin recognition complex subunit 2	3	3	0.04	-0.09	-0.04			
O43913	Origin recognition complex subunit 5	1	1	0.53	-0.02	-0.55			
P04181	Ornithine aminotransferase, mitochondrial	4	5	0.31	0.15	-0.16			
Q92882	Osteoclast-stimulating factor 1	8	76	-0.35	0.75	0.90		3	5
Q01804	OTU domain-containing protein 4	3	10	-0.15	0.20	0.36			
Q8N6M0	OTU domain-containing protein 6B	2	6	-0.01	-0.01	0.05			
Q6GQQ9	OTU domain-containing protein 7B	1	2	-0.08	0.57	0.66			
Q5BJF6	Outer dense fiber protein 2	2	3	0.19	0.14	-0.05			
Q15743	Ovarian cancer G-protein coupled receptor 1	2	2	0.46	0.72	0.24			
Q8WZ82	Ovarian cancer-associated gene 2 protein	3	8	-0.13	0.13	0.27			
Q8TAD7	Overexpressed in colon carcinoma 1 protein	1	11	-0.37	0.43	0.67			3
Q8N573	Oxidation resistance protein 1	7	11	-0.29	0.09	0.52			
Q9BUP3	Oxidoreductase HTATIP2	3	3	-0.03	0.34	0.14			
Q5BKU9	Oxidoreductase-like domain-containing protein 1	1	2	0.16	-0.29	-0.45			
P56715	Oxygen-regulated protein 1	1	3	0.24	-0.11	-0.35			
P22059	Oxysterol-binding protein 1	10	25	0.15	0.15	-0.21			
Q9BXB4	Oxysterol-binding protein-related protein 11	2	4	0.04	0.43	0.40			
Q9H4L5	Oxysterol-binding protein-related protein 3	4	6	0.13	0.28	0.24			
Q9H0X9	Oxysterol-binding protein-related protein 5	1	3	-1.87	-0.42	1.44			
Q9BZF2	Oxysterol-binding protein-related protein 7	3	9	0.08	0.28	0.21			
Q9BZF1	Oxysterol-binding protein-related protein 8	4	19	0.16	-0.07	-0.18			
Q9NWT1	p21-activated protein kinase-interacting protein 1	3	5	0.21	-0.30	-0.38			
Q96G91	P2Y purinoceptor 11	1	2	0.05	0.79	0.74			
Q9NUG6	p53 and DNA damage-regulated protein 1	1	2	-0.13	-0.20	-0.06			
Q58A45	PAB-dependent poly(A)-specific ribonuclease subunit 3	2	2	-1.52	-0.49	1.05			
Q8N7B6	PACRG-like protein	1	1	0.30	0.43	0.11			
Q96ST3	Paired amphipathic helix protein Sin3a	18	58	-0.14	-0.07	-0.03			
P50897	Palmitoyl-protein thioesterase 1	7	37	0.18	-0.18	-0.38			5
Q9C0B5	Palmitoyltransferase ZDHHC5	3	6	-0.31	0.25	0.48			
Q9BZ23	Pantothenate kinase 2, mitochondrial	2	7	0.22	0.14	-0.16			
Q9NVE7	Pantothenate kinase 4	13	46	0.24	-0.20	-0.42			
Q8NDF8	PAP-associated domain-containing protein 5	3	4	0.05	-0.11	-0.15			
Q6P1J9	Parafibromin	12	42	-0.08	0.04	0.04			
Q9UQ90	Paraplegin	2	11	0.06	-0.19	-0.13			
Q8WXF1	Paraspeckle component 1	14	83	-0.03	-0.07	-0.07			
P20962	Parathyromosin	4	33	1.10	1.15	0.09	4		4
Q8NB37	Parkinson disease 7 domain-containing protein 1	2	15	0.27	-0.26	-0.35			
Q9BRP8	Partner of Y14 and mago	9	38	0.02	-0.20	-0.05			
Q9Y5B6	PAX3- and PAX7-binding protein 1	3	8	0.08	0.10	0.06			
P49023	Paxillin	11	74	-0.72	0.17	1.06	5		5
Q6ZW49	PAX-interacting protein 1	1	1	-0.78	-0.44	0.33			
O75475	PC4 and SFRS1-interacting protein	22	132	0.13	-0.64	-0.70		5	4
Q5JVF3	PCI domain-containing protein 2	1	7	0.09	0.12	0.00			
Q9Y365	PCTP-like protein	2	3	-0.32	0.24	0.54			
O00151	PDZ and LIM domain protein 1	7	30	-1.36	-0.19	0.93	5		5
Q96JY6	PDZ and LIM domain protein 2	14	112	-0.23	0.14	0.44			
Q96HC4	PDZ and LIM domain protein 5	14	44	-0.22	0.06	0.32			
Q9NR12	PDZ and LIM domain protein 7	1	2	-1.56	-1.27	0.28			
Q5EBL8	PDZ domain-containing protein 11	1	3	0.44	0.63	0.19			
Q76G19	PDZ domain-containing protein 4	1	2	-0.45	0.51	0.94			
O14908	PDZ domain-containing protein GIPC1	2	6	-0.16	0.13	0.36			
Q8TF64	PDZ domain-containing protein GIPC3	2	3	-0.32	-1.02	-0.70			
Q9UBV8	Peflin	3	29	0.13	0.04	-0.05			
Q96EY7	Pentatricopeptide repeat domain-containing protein 3, mitochondrial	1	6	0.10	-0.02	-0.15			
Q9HBM1	Peptide deformylase, mitochondrial	1	1	0.61	-0.08	-0.68			
Q96IV0	Peptide-N(4)-(N-acetyl-beta-glucosaminyl)asparagine amidase	3	5	-0.23	-0.07	0.17			
P62937	Peptidyl-prolyl cis-trans isomerase A	15	975	-0.17	-0.24	-0.19			
P23284	Peptidyl-prolyl cis-trans isomerase B	18	180	-0.09	0.42	0.66			3
Q6UX04	Peptidyl-prolyl cis-trans isomerase CWC27 homolog	4	13	0.25	-0.39	0.11			
Q08752	Peptidyl-prolyl cis-trans isomerase D	4	22	-0.31	-0.14	0.11			
Q9UNP9	Peptidyl-prolyl cis-trans isomerase E	6	26	-0.28	-0.33	-0.02			
P30405	Peptidyl-prolyl cis-trans isomerase F, mitochondrial	8	33	-0.32	-0.18	0.16			
Q9NYL4	Peptidyl-prolyl cis-trans isomerase FKBP11	4	13	0.96	1.08	0.04		4	

P62942	Peptidyl-prolyl cis-trans isomerase FKBP1A	5	81	-0.22	-0.39	-0.25		5
P26885	Peptidyl-prolyl cis-trans isomerase FKBP2	3	18	0.28	0.65	0.28		3
Q00688	Peptidyl-prolyl cis-trans isomerase FKBP3	10	30	0.10	-0.03	-0.21		
Q02790	Peptidyl-prolyl cis-trans isomerase FKBP4	18	79	0.21	-0.08	-0.33		
Q13451	Peptidyl-prolyl cis-trans isomerase FKBP5	18	66	0.40	-0.23	-0.61		5
Q14318	Peptidyl-prolyl cis-trans isomerase FKBP8	8	26	0.04	0.03	-0.12		
Q13427	Peptidyl-prolyl cis-trans isomerase G	5	12	0.08	0.00	-0.04		
O43447	Peptidyl-prolyl cis-trans isomerase H	5	32	0.14	-0.01	-0.20		
Q13526	Peptidyl-prolyl cis-trans isomerase NIMA-interacting 1	4	14	-0.30	0.02	0.39		
Q9Y237	Peptidyl-prolyl cis-trans isomerase NIMA-interacting 4	3	15	0.05	-0.15	-0.15		
Q9Y3C6	Peptidyl-prolyl cis-trans isomerase-like 1	5	26	-0.05	-0.14	-0.12		
Q13356	Peptidyl-prolyl cis-trans isomerase-like 2	5	17	-0.39	-0.06	0.13		
Q9H2H8	Peptidyl-prolyl cis-trans isomerase-like 3	4	28	-0.17	-0.34	-0.19		
Q8WUA2	Peptidyl-prolyl cis-trans isomerase-like 4	4	11	0.13	-0.07	-0.29		
Q96BP3	Peptidylprolyl isomerase domain and WD repeat-containing protein 1	7	25	0.02	-0.26	-0.35		
Q9Y3E5	Peptidyl-tRNA hydrolase 2, mitochondrial	1	1	NA	NA	NA		
Q14197	Peptidyl-tRNA hydrolase ICT1, mitochondrial	3	4	0.08	-0.21	-0.29		
P55201	Peregrin	7	14	0.03	0.19	-0.01		
P14222	Perforin-1	18	178	-2.30	0.26	2.74	5	5
O95613	Pericentrin	11	23	0.20	-0.03	-0.26		
Q15154	Pericentriolar material 1 protein	4	6	0.24	-0.09	-0.38		
O60664	Perilipin-3	16	129	-0.55	-0.04	0.42		
Q13610	Periodic tryptophan protein 1 homolog	2	4	-0.26	-0.40	-0.14		
Q15269	Periodic tryptophan protein 2 homolog	1	1	0.15	-0.31	-0.46		
Q8NEY8	Periplakin-1	1	4	-0.11	0.11	0.07		
Q06830	Peroxisiredoxin-1	14	292	0.61	-0.22	-0.98		5
P32119	Peroxisiredoxin-2	13	339	0.89	-0.51	-1.31	5	4
Q13162	Peroxisiredoxin-4	3	79	-0.13	0.05	0.09		
P30044	Peroxisiredoxin-5, mitochondrial	12	192	-0.62	-0.12	0.52		5
P30041	Peroxisiredoxin-6	18	141	0.28	-0.33	-0.81		4
Q9NUJ1	Peroxisomal 2,4-dienoyl-CoA reductase	1	1	NA	NA	NA		
Q15067	Peroxisomal acyl-coenzyme A oxidase 1	1	1	0.00	-0.14	-0.13		
O15254	Peroxisomal acyl-coenzyme A oxidase 3	1	1	0.07	-0.05	-0.12		
P40855	Peroxisomal biogenesis factor 19	1	1	-0.42	-0.12	0.31		
O96011	Peroxisomal membrane protein 11B	1	1	0.15	0.27	0.12		
O75381	Peroxisomal membrane protein PEX14	4	7	0.00	-0.14	-0.13		
P51659	Peroxisomal multifunctional enzyme type 2	18	52	-0.06	-0.03	0.13		
Q9BY49	Peroxisomal trans-2-enoyl-CoA reductase	6	12	-0.06	-0.11	-0.23		
O75420	PERQ amino acid-rich with GYF domain-containing protein 1	1	5	-0.30	-0.33	-0.03		
Q6Y7W6	PERQ amino acid-rich with GYF domain-containing protein 2	7	13	-0.25	-0.02	0.14		
O95571	Persulfide dioxygenase ETHE1, mitochondrial	9	62	0.16	0.21	0.05		
O00541	Pescadillo homolog	7	19	0.28	-0.22	-0.29		
Q8WW12	PEST proteolytic signal-containing nuclear protein	13	64	0.07	-0.21	-0.29		
Q8NDX1	PH and SEC7 domain-containing protein 4	4	25	-0.22	0.23	0.42		
Q9P1Y6	PHD and RING finger domain-containing protein 1	5	9	-0.27	0.01	0.14		
O43189	PHD finger protein 1	2	3	0.49	-0.01	-0.49		
Q8WUB8	PHD finger protein 10	2	3	-0.13	-0.11	0.03		
Q96QT6	PHD finger protein 12	1	2	-0.18	0.20	0.39		
O94880	PHD finger protein 14	1	1	-0.06	-0.17	-0.11		
Q9BVI0	PHD finger protein 20	2	2	0.19	0.10	-0.09		
A8MW92	PHD finger protein 20-like protein 1	1	1	-2.54	-1.55	1.00		
Q96BD5	PHD finger protein 21A	1	1	0.14	0.64	0.48		
Q9BUL5	PHD finger protein 23	6	18	-0.20	-0.25	-0.16		
Q92576	PHD finger protein 3	14	23	0.08	-0.17	-0.16		
Q8IWS0	PHD finger protein 6	3	6	-0.26	-0.18	0.02		
Q7RTV0	PHD finger-like domain-containing protein 5A	4	20	-0.23	-0.35	0.16		
Q9Y285	Phenylalanine--tRNA ligase alpha subunit	11	92	0.39	-0.29	-0.78		5
Q9NSD9	Phenylalanine--tRNA ligase beta subunit	20	144	0.36	-0.19	-0.61		5
O95363	Phenylalanine--tRNA ligase, mitochondrial	1	2	0.85	0.73	-0.11		
Q8WWQ0	PH-interacting protein	10	28	0.06	-0.27	-0.32		
Q9H2J4	Phosducin-like protein 3	3	5	0.16	0.02	0.10		
O75167	Phosphatase and actin regulator 2	11	23	1.48	1.80	0.14	4	4
Q8I221	Phosphatase and actin regulator 4	3	7	-0.17	-0.15	0.15		
Q00325	Phosphate carrier protein, mitochondrial	9	54	0.18	0.26	0.02		
O95674	Phosphatidate cytidyltransferase 2	2	10	-0.03	-0.05	-0.08		
Q9UKL6	Phosphatidylcholine transfer protein	2	2	-0.94	-0.11	0.81		
P30086	Phosphatidylethanolamine-binding protein 1	12	247	0.86	-0.21	-1.06	4	4
Q8WUK0	Phosphatidylglycerophosphatase and protein-tyrosine phosphatase 1	1	2	0.22	0.06	-0.16		
Q9NTJ5	Phosphatidylinositide phosphatase SAC1	10	44	0.02	0.39	0.48		
P60484	Phosphatidylinositol 3,4,5-trisphosphate 3-phosphatase and dual-specificity	1	1	-0.22	-0.14	0.07		
Q92835	Phosphatidylinositol 3,4,5-trisphosphate 5-phosphatase 1	35	158	-0.44	0.31	0.84		5
O15357	Phosphatidylinositol 3,4,5-trisphosphate 5-phosphatase 2	5	19	-0.27	0.12	0.38		
Q8TCU6	Phosphatidylinositol 3,4,5-trisphosphate-dependent Rac exchanger 1 protein	22	78	-0.49	0.35	0.73		4
Q8NEB9	Phosphatidylinositol 3-kinase catalytic subunit type 3	6	16	-0.21	0.14	0.26		
P27986	Phosphatidylinositol 3-kinase regulatory subunit alpha	12	62	-0.12	0.14	0.13		
O00459	Phosphatidylinositol 3-kinase regulatory subunit beta	2	19	-0.23	-0.16	0.08		
P42338	Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit beta isoform	1	3	0.72	0.26	-0.46		
O00329	Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit delta isoform	8	23	0.12	-0.03	-0.39		
P48736	Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit gamma isoform	1	3	-0.51	0.17	0.68		
P42356	Phosphatidylinositol 4-kinase alpha	1	1	0.17	0.32	0.13		
Q9UBF8	Phosphatidylinositol 4-kinase beta	1	1	-0.10	0.41	0.52		
O00443	Phosphatidylinositol 4-phosphate 3-kinase C2 domain-containing subunit alpha	1	1	-0.30	-0.26	0.04		
O60331	Phosphatidylinositol 4-phosphate 5-kinase type-1 gamma	2	3	-0.17	-0.09	0.09		
P48426	Phosphatidylinositol 5-phosphate 4-kinase type-2 alpha	9	102	0.04	0.52	0.36		5
P78356	Phosphatidylinositol 5-phosphate 4-kinase type-2 beta	3	40	-0.14	0.02	0.05		
Q8TBX8	Phosphatidylinositol 5-phosphate 4-kinase type-2 gamma	8	24	-0.50	0.20	0.71		4

Q00169	Phosphatidylinositol transfer protein alpha isoform	5	21	0.11	0.24	0.16			
P48739	Phosphatidylinositol transfer protein beta isoform	6	30	0.09	0.10	0.00			
Q13492	Phosphatidylinositol-binding clathrin assembly protein	6	30	-0.50	0.15	0.59			5
Q95394	Phosphoacetylglucosamine mutase	2	2	0.35	0.17	-0.18			
Q16822	Phosphoenolpyruvate carboxykinase, mitochondrial	7	12	0.30	0.16	-0.17			
Q6VY07	Phosphofurin acidic cluster sorting protein 1	27	141	0.02	-0.14	-0.10			
Q86VP3	Phosphofurin acidic cluster sorting protein 2	3	7	-0.01	0.11	0.14			
P36871	Phosphoglucomutase-1	24	112	-0.02	0.18	0.27			
Q96G03	Phosphoglucomutase-2	13	79	-0.29	-0.08	0.06			
P00558	Phosphoglycerate kinase 1	34	1051	0.25	-0.47	-0.72		4	5
P07205	Phosphoglycerate kinase 2	2	136	0.15	-0.57	-0.70		3	4
P18669	Phosphoglycerate mutase 1	19	267	0.05	0.02	-0.09			
A6NDG6	Phosphoglycolate phosphatase	5	9	-0.28	0.01	0.43			
Q6ZUJ8	Phosphoinositide 3-kinase adapter protein 1	2	2	-0.04	1.00	1.04			
Q99570	Phosphoinositide 3-kinase regulatory subunit 4	5	10	-0.10	-0.26	-0.16			
Q96FE7	Phosphoinositide-3-kinase-interacting protein 1	1	8	-0.19	-0.56	-0.36			4
Q9Y263	Phospholipase A-2-activating protein	7	10	-0.06	0.23	0.25			
Q6P4A8	Phospholipase B-like 1	1	1	0.76	0.27	-0.49			
P36969	Phospholipid hydroperoxide glutathione peroxidase, mitochondrial	7	33	0.36	-0.11	-0.53			
Q9H008	Phospholysine phosphohistidine inorganic pyrophosphate phosphatase	7	40	0.68	-0.22	-0.91		3	5
O15305	Phosphomannomutase 2	6	18	0.26	0.19	-0.19			
Q15126	Phosphomevalonate kinase	7	26	0.14	0.47	0.21			
Q9HAB8	Phosphopantothenate--cysteine ligase	7	17	0.05	0.07	-0.07			
Q9NWQ8	Phosphoprotein associated with glycosphingolipid-enriched microdomains 1	9	19	0.57	0.08	-0.31			
Q14558	Phosphoribosyl pyrophosphate synthase-associated protein 1	7	41	0.17	0.00	-0.26			
O60256	Phosphoribosyl pyrophosphate synthase-associated protein 2	8	61	0.06	-0.31	-0.28			
O15067	Phosphoribosylformylglycinamidine synthase	16	30	0.02	-0.22	-0.26			
P15735	Phosphorylase b kinase gamma catalytic chain, liver/testis isoform	1	1	NA	NA	NA			
P46019	Phosphorylase b kinase regulatory subunit alpha, liver isoform	5	7	0.12	0.12	-0.02			
Q9H814	Phosphorylated adapter RNA export protein	4	10	-0.13	-0.38	-0.24			
Q9H423	Phosphorylated CTD-interacting factor 1	2	2	-0.21	-0.18	0.03			
Q9Y617	Phosphoserine aminotransferase	2	3	0.02	-0.87	-0.90			
P78330	Phosphoserine phosphatase	1	1	-0.08	-0.25	-0.17			
Q96BW5	Phosphotriesterase-related protein	7	20	-0.11	-0.29	-0.12			
Q6NYC8	Phostensin	22	112	-0.48	0.33	0.77			5
P36955	Pigment epithelium-derived factor	1	4	0.65	0.77	0.01			
Q9NWS0	PIH1 domain-containing protein 1	4	8	-0.07	-0.32	-0.26			
Q96BK5	PIN2/TERF1-interacting telomerase inhibitor 1	4	13	-0.02	-0.11	-0.20			
Q9H307	Pinin	17	62	-0.21	-0.17	-0.07			
Q9GZP4	PITH domain-containing protein 1	9	25	0.29	-0.02	-0.24			
P20020	Plasma membrane calcium-transporting ATPase 1	3	42	0.42	0.46	0.05			
P23634	Plasma membrane calcium-transporting ATPase 4	9	82	0.38	0.98	0.72		5	5
Q8NC51	Plasminogen activator inhibitor 1 RNA-binding protein	21	99	0.19	-0.25	-0.31			
P05120	Plasminogen activator inhibitor 2	3	4	-0.10	0.03	0.20			
Q9HBL7	Plasminogen receptor (KT)	1	15	-0.06	-0.09	-0.16			
Q14651	Plastin-1	1	172	1.08	0.62	-0.45			
P13796	Plastin-2	40	1792	0.04	0.51	0.34			
P13797	Plastin-3	1	395	-0.34	0.28	0.42			
P02775	Platelet basic protein	6	35	0.00	-0.12	0.03			
P16284	Platelet endothelial cell adhesion molecule	7	16	-0.16	-0.47	-0.40			5
P02776	Platelet factor 4	4	14	0.12	-0.14	-0.47			
P16671	Platelet glycoprotein 4	1	1	-0.01	-0.07	-0.05			
P07359	Platelet glycoprotein Ib alpha chain	3	7	NA	NA	NA			
P13224	Platelet glycoprotein Ib beta chain	1	1	NA	NA	NA			
P14770	Platelet glycoprotein IX	1	1	-0.20	-0.18	0.01			
Q9H7M9	Platelet receptor G124	2	3	0.13	0.49	0.37			
Q99487	Platelet-activating factor acetylhydrolase 2, cytoplasmic	1	1	-0.71	-0.13	0.58			
P43034	Platelet-activating factor acetylhydrolase IB subunit alpha	11	44	0.26	0.15	-0.05			
P68402	Platelet-activating factor acetylhydrolase IB subunit beta	2	58	0.24	-0.25	-0.64			4
Q15102	Platelet-activating factor acetylhydrolase IB subunit gamma	8	41	0.74	-0.24	-0.96		5	5
P08567	Pleckstrin	10	32	-0.72	0.23	0.71		3	4
Q9HB21	Pleckstrin homology domain-containing family A member 1	4	18	-0.37	-0.15	0.56			4
Q9HB19	Pleckstrin homology domain-containing family A member 2	7	30	-0.26	0.13	0.39			5
Q96599	Pleckstrin homology domain-containing family F member 1	1	15	-0.44	0.77	1.11			3
Q9H8W4	Pleckstrin homology domain-containing family F member 2	1	12	0.13	-0.02	-0.14			
Q9Y4G2	Pleckstrin homology domain-containing family M member 1	1	1	0.19	0.10	-0.08			
Q8IWE5	Pleckstrin homology domain-containing family M member 2	2	2	-0.17	-0.22	-0.04			
Q53GL0	Pleckstrin homology domain-containing family O member 1	1	2	0.22	0.01	-0.20			
Q8TD55	Pleckstrin homology domain-containing family O member 2	10	33	-0.40	0.25	0.70			5
Q15149	Plectin	197	1024	0.64	0.01	-0.75		5	5
O43660	Pleiotropic regulator 1	10	28	-0.14	-0.10	0.02			
O15031	Plexin-B2	1	1	0.10	-0.20	-0.29			
O00592	Podocalyxin	1	1	1.03	1.26	0.22			
Q7Z3K3	Pogo transposable element with ZNF domain	8	19	-0.17	-0.08	0.06			
P09874	Poly polymerase 1	48	387	0.43	-0.03	-0.42			
Q53GL7	Poly polymerase 10	9	29	-0.22	0.09	0.39			
Q9H0J9	Poly polymerase 12	5	14	-0.12	0.11	0.21			
Q460N5	Poly polymerase 14	11	17	-0.03	0.17	0.24			
Q9UGN5	Poly polymerase 2	1	1	-0.10	-0.18	-0.09			
Q9UKK3	Poly polymerase 4	3	8	-0.37	-0.11	0.29			
Q8N3A8	Poly polymerase 8	1	1	0.32	0.52	0.20			
Q8IXQ6	Poly polymerase 9	3	10	0.14	0.08	-0.09			
P51003	Poly(A) polymerase alpha	6	45	-0.06	-0.05	0.10			
Q9BWT3	Poly(A) polymerase gamma	2	12	-0.15	-0.04	0.05			
Q9NVV4	Poly(A) RNA polymerase, mitochondrial	1	2	NA	NA	NA			
O95453	Poly(A)-specific ribonuclease PARN	5	6	0.07	-0.10	-0.16			

Q9NX46	Poly(ADP-ribose) glycohydrolase ARH3	10	54	-0.01	-0.20	-0.23			
Q15365	Poly(rC)-binding protein 1	10	318	-0.13	-0.08	-0.03			
Q15366	Poly(rC)-binding protein 2	5	211	-0.02	-0.25	-0.26			
P57721	Poly(rC)-binding protein 3	1	126	0.16	0.11	-0.04			
P57723	Poly(rC)-binding protein 4	1	21	0.75	-0.46	-1.20			
Q9UHX1	Poly(U)-binding-splicing factor PUF60	20	119	0.03	-0.20	-0.20			
P11940	Polyadenylate-binding protein 1	24	288	0.16	0.16	-0.06			
Q86U42	Polyadenylate-binding protein 2	9	36	-0.29	-0.17	0.07			
Q13310	Polyadenylate-binding protein 4	7	88	0.12	-0.23	-0.39			
Q9H074	Polyadenylate-binding protein-interacting protein 1	1	1	NA	NA	NA			
Q9BPZ3	Polyadenylate-binding protein-interacting protein 2	1	1	0.28	0.01	-0.27			
P35226	Polycomb complex protein BMI-1	2	3	0.53	0.20	-0.22			
O75530	Polycomb protein EED	1	1	0.32	0.10	-0.21			
Q15022	Polycomb protein SUZ12	2	7	-0.38	-0.07	0.17			
O60828	Polyglutamine-binding protein 1	6	26	-0.28	-0.31	-0.01			
Q8NDX5	Polyhomeotic-like protein 3	4	9	0.36	0.05	-0.16			
Q9Y257	Polymerase delta-interacting protein 2	1	3	-0.15	-0.13	0.02			
Q9BY77	Polymerase delta-interacting protein 3	14	68	-0.20	-0.09	0.16			
P01833	Polymeric immunoglobulin receptor	1	2	0.94	1.53	0.60			
Q5SY16	Polynucleotide 5'-hydroxyl-kinase NOL9	3	3	0.19	0.04	-0.14			
Q10472	Polypeptide N-acetylglucosaminyltransferase 1	1	1	-0.01	0.80	0.81			
Q8IUC8	Polypeptide N-acetylglucosaminyltransferase 13	1	11	-0.99	-0.32	0.68	3		
P26599	Polypyrimidine tract-binding protein 1	16	177	0.01	-0.18	-0.18			
O95758	Polypyrimidine tract-binding protein 3	7	87	0.05	-0.11	-0.27			
Q9Z989	Polyribonucleotide 5'-hydroxyl-kinase Clp1	1	2	0.22	0.16	-0.07			
Q8TCS8	Polyribonucleotide nucleotidyltransferase 1, mitochondrial	14	26	0.47	-0.02	-0.32			
P08397	Porphobilinogen deaminase	3	4	0.18	-0.39	-0.45			
P14859	POU domain, class 2, transcription factor 1	2	5	-0.13	0.14	0.33			
O60831	PRA1 family protein 2	1	8	0.16	0.26	0.15			
O75915	PRA1 family protein 3	4	80	-0.09	-0.16	0.01			
P40425	Pre-B-cell leukemia transcription factor 2	1	2	-0.41	-0.27	0.14			
Q96AQ6	Pre-B-cell leukemia transcription factor-interacting protein 1	9	24	0.61	0.62	-0.01		5	
O60925	Prefoldin subunit 1	4	23	-0.20	-0.24	-0.10			
Q9UHV9	Prefoldin subunit 2	7	36	-0.12	-0.32	-0.17			
P61758	Prefoldin subunit 3	7	19	-0.03	-0.08	-0.09			
Q9NQP4	Prefoldin subunit 4	5	21	-0.18	-0.30	-0.15			
Q99471	Prefoldin subunit 5	6	28	-0.13	-0.41	-0.15			
O15212	Prefoldin subunit 6	6	29	-0.24	-0.31	0.00			
P02545	Prelamin-A/C	43	347	0.69	0.88	0.18	4		4
Q9C0J8	pre-mRNA 3' end processing protein WDR33	17	28	-0.09	-0.03	-0.04			
Q6UN15	Pre-mRNA 3'-end-processing factor FIP1	9	44	0.02	-0.06	0.02			
Q9Y3B4	Pre-mRNA branch site protein p14	5	16	-0.17	0.03	0.07			
O94913	Pre-mRNA cleavage complex 2 protein Pcf11	2	2	0.38	0.22	-0.15			
O60508	Pre-mRNA-processing factor 17	7	17	-0.20	-0.04	0.10			
Q9UMS4	Pre-mRNA-processing factor 19	13	48	-0.18	-0.05	0.06			
Q86UA1	Pre-mRNA-processing factor 39	2	5	0.20	-0.15	-0.28			
O75400	Pre-mRNA-processing factor 40 homolog A	14	65	-0.24	-0.09	-0.07			
O94906	Pre-mRNA-processing factor 6	23	71	-0.14	-0.10	-0.02			
Q6P2Q9	Pre-mRNA-processing-splicing factor 8	43	148	0.06	-0.08	-0.05			
Q8NAV1	Pre-mRNA-splicing factor 38A	3	11	-0.15	-0.26	-0.10			
Q5VTL8	Pre-mRNA-splicing factor 38B	3	7	0.09	0.10	0.00			
Q92620	Pre-mRNA-splicing factor ATP-dependent RNA helicase PRP16	7	26	0.03	0.16	0.10			
Q9NXE8	Pre-mRNA-splicing factor CWC25 homolog	2	4	-0.10	0.02	0.12			
Q9ULR0	Pre-mRNA-splicing factor ISY1 homolog	5	33	-0.27	-0.21	0.15			
Q9NW64	Pre-mRNA-splicing factor RBM22	5	29	-0.03	0.12	0.10			
O95391	Pre-mRNA-splicing factor SLU7	2	3	0.09	-0.03	-0.11			
O75934	Pre-mRNA-splicing factor SPF27	6	21	-0.30	-0.20	0.05			
Q9HCS7	Pre-mRNA-splicing factor SYF1	7	18	0.00	-0.04	-0.18			
O95926	Pre-mRNA-splicing factor SYF2	2	3	-0.14	0.10	0.25			
Q15007	Pre-mRNA-splicing regulator WTAP	8	35	-0.25	-0.18	0.07			
Q9UHG3	Preylcysteine oxidase 1	5	6	0.40	-0.11	-0.64			
Q8IY81	pre-rRNA processing protein FTSJ3	13	52	0.33	-0.11	-0.42			5
Q2NL82	Pre-rRNA-processing protein TSR1 homolog	4	8	0.35	0.18	-0.33			
Q969E8	Pre-rRNA-processing protein TSR2 homolog	2	2	0.03	0.15	0.09			
Q5JRX3	Presequence protease, mitochondrial	14	25	0.14	-0.12	-0.22			
Q9H875	PRKR-interacting protein 1	5	26	-0.26	-0.12	-0.02			
Q8NDH3	Probable aminopeptidase NPEPL1	4	12	0.18	0.30	0.26			
Q5T160	Probable arginine--tRNA ligase, mitochondrial	1	1	-0.02	0.05	0.05			
Q96159	Probable asparagine--tRNA ligase, mitochondrial	1	1	0.94	0.01	-0.95			
Q13206	Probable ATP-dependent RNA helicase DDX10	2	5	0.18	-0.29	-0.55			
Q92841	Probable ATP-dependent RNA helicase DDX17	28	394	-0.05	-0.06	-0.08			
Q9UHT6	Probable ATP-dependent RNA helicase DDX20	2	2	0.62	-0.21	-0.83			
Q9BUQ8	Probable ATP-dependent RNA helicase DDX23	17	87	-0.25	-0.17	0.04			
Q96GQ7	Probable ATP-dependent RNA helicase DDX27	18	51	0.34	-0.17	-0.54			5
Q9NUL7	Probable ATP-dependent RNA helicase DDX28	2	2	0.93	-0.07	-1.00			
Q9UJV9	Probable ATP-dependent RNA helicase DDX41	8	13	0.03	-0.19	-0.15			
Q7L014	Probable ATP-dependent RNA helicase DDX46	34	150	-0.11	-0.07	0.00			
Q9H0S4	Probable ATP-dependent RNA helicase DDX47	8	26	0.69	-0.26	-1.07	5		5
Q9Y6V7	Probable ATP-dependent RNA helicase DDX49	1	1	NA	NA	NA			
P17844	Probable ATP-dependent RNA helicase DDX5	17	222	-0.03	-0.11	0.09			
Q9Y2R4	Probable ATP-dependent RNA helicase DDX52	1	4	0.41	-0.09	-0.56			
Q9NY93	Probable ATP-dependent RNA helicase DDX56	4	15	0.19	-0.21	-0.33			
O95786	Probable ATP-dependent RNA helicase DDX58	7	22	0.15	0.18	0.01			
Q5T1V6	Probable ATP-dependent RNA helicase DDX59	2	18	-0.19	-0.11	0.08			
P26196	Probable ATP-dependent RNA helicase DDX6	13	74	-0.17	0.17	0.03			
Q8TY21	Probable ATP-dependent RNA helicase DDX60	15	50	0.38	0.11	-0.33			

Q5H9U9	Probable ATP-dependent RNA helicase DDX60-like	1	1	-0.01	0.16	0.17			
Q14147	Probable ATP-dependent RNA helicase DHX34	2	2	-0.28	-0.03	0.25			
Q9H5Z1	Probable ATP-dependent RNA helicase DHX35	2	3	-0.93	0.14	1.05			
Q9H2U1	Probable ATP-dependent RNA helicase DHX36	8	11	-0.01	-0.07	0.01			
Q8IY37	Probable ATP-dependent RNA helicase DHX37	5	9	-0.03	-0.29	-0.25			
Q8IX18	Probable ATP-dependent RNA helicase DHX40	2	3	NA	NA	NA			
Q9H6S0	Probable ATP-dependent RNA helicase YTHDC2	2	2	-0.51	-0.24	0.25			
Q9HD20	Probable cation-transporting ATPase 13A1	6	12	0.20	0.22	0.02			
Q9HA77	Probable cysteine--tRNA ligase, mitochondrial	2	6	0.15	-0.06	-0.23			
O76071	Probable cytosolic iron-sulfur protein assembly protein CIAO1	3	5	0.05	-0.02	-0.07			
Q9UNQ2	Probable dimethyladenosine transferase	2	6	0.28	-0.26	-0.52			
Q5GLZ8	Probable E3 ubiquitin-protein ligase HERC4	4	12	0.08	-0.10	-0.14			
Q9H000	Probable E3 ubiquitin-protein ligase makorin-2	1	1	0.00	0.05	0.05			
O75592	Probable E3 ubiquitin-protein ligase MYCBP2	21	35	0.08	-0.31	-0.42			
Q9HAH7	Probable fibrosin-1	1	1	0.09	0.47	0.40			
P51531	Probable global transcription activator SNF2L2	14	96	-0.12	-0.15	0.03			
Q5T6J7	Probable gluconokinase	1	1	-1.02	-0.73	0.27			
Q7Z333	Probable helicase senataxin	5	11	-0.08	-0.31	0.11			
P42694	Probable helicase with zinc finger domain	3	10	-0.37	0.36	0.98			3
P49590	Probable histidine--tRNA ligase, mitochondrial	2	23	0.18	0.09	0.07			
Q15652	Probable JmjC domain-containing histone demethylation protein 2C	2	5	0.28	0.16	-0.18			
Q15031	Probable leucine--tRNA ligase, mitochondrial	1	5	0.08	0.09	0.10			
Q9NUN5	Probable lysosomal cobalamin transporter	1	2	0.49	0.28	-0.20			
Q13395	Probable methyltransferase TARBP1	1	2	0.33	-0.30	-0.63			
Q5W0Z9	Probable palmitoyltransferase ZDHHC20	2	6	-0.15	0.31	0.46			
Q86Y79	Probable peptidyl-tRNA hydrolase	1	2	0.09	-0.43	-0.50			
Q9Y2Q0	Probable phospholipid-transporting ATPase IA	2	2	0.00	0.22	0.22			
Q9Y2G3	Probable phospholipid-transporting ATPase IF	2	6	-0.25	0.28	0.53			
Q9P241	Probable phospholipid-transporting ATPase VD	1	1	NA	NA	NA			
Q7L3T8	Probable proline--tRNA ligase, mitochondrial	1	1	0.22	0.18	-0.04			
Q9UHA3	Probable ribosome biogenesis protein RLP24	2	4	0.19	-0.42	-0.74			
Q96CW6	Probable RNA polymerase II nuclear localization protein SLC7A6OS	1	1	0.06	0.15	0.09			
Q9Y4C8	Probable RNA-binding protein 19	4	11	0.32	-0.13	-0.44			
Q86U06	Probable RNA-binding protein 23	1	5	-0.69	-0.02	0.67			
Q8N9N8	Probable RNA-binding protein EIF1AD	2	4	-0.03	-0.15	-0.12			
Q99848	Probable rRNA-processing protein EBP2	8	29	0.54	-0.07	-0.44			5
A2RTX5	Probable threonine--tRNA ligase 2, cytoplasmic	2	3	0.05	0.06	0.02			
Q9NPF4	Probable tRNA N6-adenosine threonylcarbamoyltransferase	9	53	-0.07	-0.11	0.01			
Q8WWH5	Probable tRNA pseudouridine synthase 1	4	14	-0.14	0.00	0.05			
Q9Y3A2	Probable U3 small nucleolar RNA-associated protein 11	2	3	0.34	0.10	-0.23			
Q93008	Probable ubiquitin carboxyl-terminal hydrolase FAF-X	13	31	0.25	0.33	-0.02			
Q9NQH7	Probable Xaa-Pro aminopeptidase 3	1	2	0.20	-0.30	-0.49			
P09668	Pro-cathepsin H	2	8	1.92	2.11	0.17	4		4
Q8NBJ5	Procollagen galactosyltransferase 1	1	1	-0.34	0.43	0.78			
O60568	Procollagen-lysine,2-oxoglutarate 5-dioxygenase 3	1	6	-0.22	0.38	0.56			
P07737	Profilin-1	16	1786	-0.42	-0.16	0.28			
P35080	Profilin-2	3	14	0.68	-0.33	-1.26	5		5
Q8WXW3	Progesterone-induced-blocking factor 1	1	1	-0.14	-0.07	0.07			
Q8WUM4	Programmed cell death 6-interacting protein	37	196	0.25	0.05	-0.09			
Q9BUL8	Programmed cell death protein 10	7	28	-0.03	0.09	0.06			
Q16342	Programmed cell death protein 2	1	1	1.21	0.15	-1.05			
Q53EL6	Programmed cell death protein 4	24	222	0.93	0.37	-0.50	5		5
O14737	Programmed cell death protein 5	7	49	0.22	-0.01	-0.37			
O75340	Programmed cell death protein 6	4	8	0.61	-0.14	-0.90			
Q8N8D1	Programmed cell death protein 7	1	1	0.45	-0.01	-0.45			
P35232	Prohibitin	19	294	0.19	0.14	-0.05			
Q99623	Prohibitin-2	20	213	0.19	0.20	-0.01			
Q14005	Pro-interleukin-16	34	370	-0.08	-0.39	-0.20			
Q9HCU5	Prolactin regulatory element-binding protein	3	3	0.67	0.03	-0.63			
P12273	Prolactin-inducible protein	1	1	-1.50	-1.01	0.50			
P12004	Proliferating cell nuclear antigen	13	50	-0.06	0.05	0.13			
Q9UQ80	Proliferation-associated protein 2G4	22	204	0.18	0.10	-0.13			
O94903	Proline synthase co-transcribed bacterial homolog protein	10	61	-0.02	-0.18	-0.20			
Q8IZL8	Proline-, glutamic acid- and leucine-rich protein 1	5	8	0.11	-0.11	-0.11			
Q9ULL5	Proline-rich protein 12	3	6	0.05	0.16	0.33			
Q9BWN1	Proline-rich protein 14	2	3	-0.29	0.56	0.58			
Q16378	Proline-rich protein 4	1	2	NA	NA	NA			
P85299	Proline-rich protein 5	1	4	0.17	0.28	0.11			
Q92733	Proline-rich protein PRCC	5	41	-0.31	-0.16	0.10			
O43586	Proline-serine-threonine phosphatase-interacting protein 1	12	44	-0.15	0.49	0.63	5		4
Q9H939	Proline-serine-threonine phosphatase-interacting protein 2	3	4	-1.19	-0.56	0.61			
P13674	Prolyl 4-hydroxylase subunit alpha-1	1	1	0.48	0.46	0.00			
P48147	Prolyl endopeptidase	11	45	0.01	0.22	0.28			
P05165	Propionyl-CoA carboxylase alpha chain, mitochondrial	10	21	0.24	0.12	-0.16			
P05166	Propionyl-CoA carboxylase beta chain, mitochondrial	8	21	0.12	-0.06	-0.14			
P07602	Prosaposin	2	8	-0.60	0.04	0.73			
Q9H7Z7	Prostaglandin E synthase 2	9	30	0.13	0.14	-0.05			
Q15185	Prostaglandin E synthase 3	5	14	0.39	0.18	-0.20			
Q8N8N7	Prostaglandin reductase 2	1	1	-0.18	-0.48	-0.30			
P41222	Prostaglandin-H2 D-isomerase	1	1	NA	NA	NA			
Q8TBF2	Prostamide/prostaglandin F synthase	1	2	0.19	-0.27	-0.46			
Q9BRP4	Proteasomal ATPase-associated factor 1	3	7	-0.27	0.06	0.19			
Q16186	Proteasomal ubiquitin receptor ADRM1	4	22	0.11	-0.01	-0.07			
Q06323	Proteasome activator complex subunit 1	13	182	-0.02	0.10	0.04			
Q9UL46	Proteasome activator complex subunit 2	9	76	0.34	0.26	-0.16			
P61289	Proteasome activator complex subunit 3	8	28	-0.26	0.05	0.27			

Q14997	Proteasome activator complex subunit 4	1	1	NA	NA	NA			
O95456	Proteasome assembly chaperone 1	2	3	-0.28	-0.20	-0.35			
Q969U7	Proteasome assembly chaperone 2	1	1	0.20	-0.22	-0.42			
Q9BT73	Proteasome assembly chaperone 3	1	1	0.06	-0.08	-0.14			
Q5J554	Proteasome assembly chaperone 4	1	1	-0.51	-0.96	-0.47			
Q92530	Proteasome inhibitor PI31 subunit	3	12	0.14	-0.26	-0.18			
P25786	Proteasome subunit alpha type-1	18	146	-0.09	-0.09	-0.09			
P25787	Proteasome subunit alpha type-2	10	84	-0.07	-0.02	0.00			
P25788	Proteasome subunit alpha type-3	11	100	0.19	-0.01	-0.12			
P25789	Proteasome subunit alpha type-4	9	42	0.23	0.06	-0.13			
P28066	Proteasome subunit alpha type-5	8	126	0.01	-0.06	-0.15			
P60900	Proteasome subunit alpha type-6	14	149	0.01	0.06	0.04			
O14818	Proteasome subunit alpha type-7	16	135	0.13	-0.11	-0.17			
P20618	Proteasome subunit beta type-1	11	76	0.08	0.09	-0.04			
P40306	Proteasome subunit beta type-10	10	68	-0.18	-0.13	0.01			
P49721	Proteasome subunit beta type-2	4	8	0.08	-0.03	-0.15			
P49720	Proteasome subunit beta type-3	6	46	0.15	0.12	-0.03			
P28070	Proteasome subunit beta type-4	8	112	-0.02	-0.01	0.05			
P28072	Proteasome subunit beta type-6	2	2	NA	NA	NA			
Q99436	Proteasome subunit beta type-7	2	6	-0.14	-0.25	-0.18			
P28062	Proteasome subunit beta type-8	12	74	-0.09	-0.03	0.00			
P28065	Proteasome subunit beta type-9	9	130	-0.10	-0.05	0.01			
Q5VYK3	Proteasome-associated protein ECM29 homolog	15	39	0.45	0.40	-0.09			
Q9NUX5	Protection of telomeres protein 1	1	1	-0.71	-0.07	0.65			
P11171	Protein 4.1	22	103	0.30	-0.07	-0.27			
Q9NY61	Protein AATF	5	11	0.15	-0.26	-0.66			3
P55197	Protein AF-10	1	1	0.03	-0.31	-0.34			
P55198	Protein AF-17	3	4	0.09	0.23	0.13			
Q5VTE6	Protein angel homolog 2	1	1	-0.04	0.05	0.09			
Q8IWT0	Protein archease	1	1	NA	NA	NA			
Q99873	Protein arginine N-methyltransferase 1	6	11	0.07	-0.05	0.00			
O14744	Protein arginine N-methyltransferase 5	6	9	0.80	0.03	-0.78	5		5
Q9UL18	Protein argonaute-1	5	32	0.16	-0.17	-0.21			
Q9UKV8	Protein argonaute-2	8	35	0.03	0.07	0.08			
Q9H9G7	Protein argonaute-3	2	26	-0.28	-0.17	0.10			
Q9NVM9	Protein asunder homolog	4	6	0.12	0.07	-0.19			
Q8N9N5	Protein BANP	1	4	-0.08	0.14	0.17			
Q8TD16	Protein bicaudal D homolog 2	4	10	-0.07	0.16	0.24			
Q8WUW1	Protein BRICK1	6	24	-0.14	0.16	0.47			
P41223	Protein BUD31 homolog	5	7	0.11	0.15	0.08			
Q99622	Protein C10	2	4	-0.19	0.20	-0.32			
Q9Y2B0	Protein canopy homolog 2	4	21	0.05	0.13	-0.02			
Q9BT09	Protein canopy homolog 3	10	27	-0.34	-0.35	-0.05			
Q8N129	Protein canopy homolog 4	4	4	0.00	-0.26	-0.43			
Q96RK0	Protein capicua homolog	1	2	-0.21	0.03	0.25			
O15234	Protein CASC3	3	4	-0.74	-0.24	0.51			
Q13948	Protein CASP	1	2	-0.48	-0.06	0.42			
Q9UKY7	Protein CDV3 homolog	9	84	0.12	-0.16	-0.44			
Q96SW2	Protein cereblon	1	2	-0.27	-0.47	-0.21			
P14921	Protein C-ets-1	7	15	0.12	-0.29	-0.49			
Q8WUH1	Protein Churchill	1	3	-0.74	0.12	0.87			
Q2KHT3	Protein CLEC16A	1	1	-0.23	0.20	0.42			
Q9BQ75	Protein CMSS1	3	3	0.19	-0.45	-0.63			
Q5IJ48	Protein crumbs homolog 2	1	1	NA	NA	NA			
O60888	Protein CutA	3	46	-0.58	-0.13	-0.06			
Q96DE9	Protein CXorf40B	1	1	0.08	0.57	0.50			
Q9P219	Protein Daple	8	13	-0.13	-0.09	0.38			
Q5TDH0	Protein DDI1 homolog 2	10	45	0.08	-0.05	-0.24			
P35659	Protein DEK	14	131	0.17	0.14	0.00			
P80370	Protein delta homolog 1	1	8	-0.02	-0.15	-0.01			
Q96DF8	Protein DGCR14	3	6	-0.15	0.22	0.37			
O60610	Protein diaphanous homolog 1	39	201	-0.10	-0.15	0.11			
O60879	Protein diaphanous homolog 2	2	3	0.52	0.32	-0.20			
P07237	Protein disulfide-isomerase	32	272	0.05	0.61	0.56	5		4
P30101	Protein disulfide-isomerase A3	40	571	-0.29	0.40	0.67			4
P13667	Protein disulfide-isomerase A4	30	256	0.06	0.56	0.47	4		4
Q14554	Protein disulfide-isomerase A5	2	4	0.41	0.06	-0.09			
Q15084	Protein disulfide-isomerase A6	14	195	-0.15	0.78	0.82	5		4
Q96JJ7	Protein disulfide-isomerase TMX3	3	15	0.00	0.30	0.42			
Q99497	Protein DJ-1	16	265	-0.12	-0.20	-0.06			
Q5JWR5	Protein dopey-1	1	1	NA	NA	NA			
Q9Y3R5	Protein dopey-2	1	6	0.10	0.10	0.01			
Q9C005	Protein dpy-30 homolog	3	5	-0.13	-0.08	-0.05			
Q01658	Protein Dr1	5	26	-0.20	-0.20	0.19			
Q14156	Protein EFR3 homolog A	2	3	0.53	0.57	0.05			
Q8WYP5	Protein ELYS	23	64	-0.14	-0.01	0.15			
Q7Z589	Protein EMSY	9	15	-0.13	-0.05	0.06			
Q03111	Protein ENL	1	1	-0.09	-0.16	-0.07			
P49257	Protein ERGIC-53	6	22	0.17	0.53	0.01	3		
P34910	Protein EVI2B	1	3	0.41	0.07	0.09			
Q13158	Protein FADD	2	2	0.27	-0.25	-0.52			
Q8N5W9	Protein FAM101B	2	4	0.42	-0.28	-0.70			3
Q5T9C2	Protein FAM102A	2	5	0.67	-0.19	-0.73			3
Q969W3	Protein FAM104A	1	6	-0.36	0.07	0.50			
Q9H098	Protein FAM107B	9	23	0.23	-0.18	-0.04			
Q9NRY5	Protein FAM114A2	4	12	0.07	0.09	-0.07			

A6NFQ2	Protein FAM115C	1	1	0.47	0.01	-0.45			
Q6P1L5	Protein FAM117B	1	1	-0.03	-1.35	-1.34			
Q5BKY9	Protein FAM133B	2	4	-0.26	-0.18	-0.03			
Q8NC44	Protein FAM134A	1	3	0.58	0.20	-0.37			
Q86VR2	Protein FAM134C	2	3	-0.18	0.03	0.20			
Q9P2D6	Protein FAM135A	1	1	NA	NA	NA			
Q96C01	Protein FAM136A	3	15	-0.43	-0.10	0.40			
Q8WW52	Protein FAM151A	1	1	NA	NA	NA			
Q92567	Protein FAM168A	1	1	-0.45	-0.40	0.03			
Q8WUF8	Protein FAM172A	5	8	-0.15	-0.05	0.08			
Q8N128	Protein FAM177A1	1	5	-0.37	-0.10	0.37			
Q9GZU8	Protein FAM192A	3	7	-0.19	-0.14	0.03			
C9JLW8	Protein FAM195B	4	8	-0.73	-0.15	0.69			
Q6UWH4	Protein FAM198B	1	1	NA	NA	NA			
P0CB43	Protein FAM203B	4	13	-0.09	-0.12	-0.14			
Q9NSI2	Protein FAM207A	2	6	0.25	0.13	-0.12			
Q9UK61	Protein FAM208A	5	6	0.48	0.19	-0.04			
Q5VWN6	Protein FAM208B	1	1	NA	NA	NA			
Q9Y421	Protein FAM32A	3	11	-0.08	-0.40	-0.41			
Q92520	Protein FAM3C	3	4	-0.17	0.27	0.50			
Q6NSW5	Protein FAM45B	2	3	0.31	0.09	-0.20			
Q9NUQ9	Protein FAM49B	16	133	-0.50	0.25	0.74			4
Q14320	Protein FAM50A	4	5	0.19	0.33	0.00			
Q9Y4F9	Protein FAM65B	7	28	-0.03	-0.04	0.02			
Q8TAV0	Protein FAM76A	1	1	-1.57	-1.10	0.49			
Q5HYJ3	Protein FAM76B	2	2	-1.42	-0.83	0.59			
Q96KN1	Protein FAM84B	1	1	-0.07	-0.19	-0.13			
Q8N7N1	Protein FAM86B1	1	2	NA	NA	NA			
Q658Y4	Protein FAM91A1	1	1	-0.12	0.43	0.55			
Q8NCA5	Protein FAM98A	2	12	-0.05	0.00	0.07			
Q52LJ0	Protein FAM98B	4	71	0.18	-0.23	-0.37			
Q17RN3	Protein FAM98C	2	2	0.11	-0.31	-0.40			
P49354	Protein farnesyltransferase/geranylgeranyltransferase type-1 subunit alpha	1	3	0.22	0.44	0.22			
Q13045	Protein flightless-1 homolog	19	97	0.06	0.12	0.00			
Q70Z53	Protein FRA10AC1	1	1	-1.46	-1.34	0.13			
Q14331	Protein FRG1	5	14	-0.16	-0.04	-0.04			
O94915	Protein furry homolog-like	9	16	-0.09	0.00	0.01			
O94992	Protein HEXIM1	1	2	-2.42	-1.23	1.20			
Q9UJC3	Protein Hook homolog 1	4	5	0.08	-0.66	-0.69			
Q86VS8	Protein Hook homolog 3	10	32	-0.14	-0.02	0.16			
Q9P2X3	Protein IMPACT	1	5	0.07	-0.31	-0.38			
Q96ST2	Protein IWS1 homolog	3	5	-0.16	-0.19	-0.03			
Q9NQC1	Protein Jade-2	2	7	-0.02	-0.14	-0.19			
Q8NSM9	Protein jagunal homolog 1	1	7	0.14	0.04	-0.07			
O15037	Protein KHNYN	1	1	0.11	0.13	0.01			
P17252	Protein kinase C alpha type	4	31	0.30	-0.95	-1.24		5	5
Q9BY11	Protein kinase C and casein kinase substrate in neurons protein 1	2	3	-0.11	0.30	0.47			
Q9UNF0	Protein kinase C and casein kinase substrate in neurons protein 2	7	22	-0.06	-0.05	0.03			
P05771	Protein kinase C beta type	10	46	-0.05	-0.01	-0.06			
Q05655	Protein kinase C delta type	8	23	-0.10	0.37	0.43			
P24723	Protein kinase C eta type	8	42	-0.57	0.01	0.39			
Q04759	Protein kinase C theta type	2	3	-0.01	-0.04	-0.04			
Q9ULU4	Protein kinase C-binding protein 1	3	5	-0.03	0.02	0.08			
Q92832	Protein kinase C-binding protein NELL1	1	1	-0.24	0.00	0.23			
Q8N9T8	Protein KRI1 homolog	6	19	0.11	-0.12	-0.24			
Q96EK9	Protein KTI12 homolog	2	4	-0.27	-0.06	0.19			
Q96RT1	Protein LAP2	9	23	-0.27	0.09	0.49			
Q53QV2	Protein LBH	4	7	-0.59	0.40	0.99			
Q96GY3	Protein lin-37 homolog	1	4	-0.07	-0.19	-0.12			
Q6MZP7	Protein lin-54 homolog	4	6	-0.47	-0.06	0.47			
Q9NUP9	Protein lin-7 homolog C	3	13	0.09	-0.06	-0.15			
Q3MHD2	Protein LSM12 homolog	1	3	-0.11	-0.16	-0.07			
Q8ND56	Protein LSM14 homolog A	2	28	-0.26	-0.26	0.01			
Q9BX40	Protein LSM14 homolog B	1	29	-0.25	0.09	0.35			
Q96GA3	Protein LTV1 homolog	2	3	-0.30	-0.22	0.07			
Q9C0E8	Protein lunapark	2	10	0.03	0.36	0.31			
Q86UE4	Protein LYRIC	14	82	0.45	0.16	-0.16			
Q8WZA0	Protein LZIC	4	8	-0.31	-0.09	0.36			
P61326	Protein mago nashi homolog	6	17	0.01	-0.12	-0.13			
Q9BXY0	Protein MAK16 homolog	2	2	-0.12	-0.35	-0.25			
P61244	Protein max	5	17	-0.34	-0.62	-0.09		3	
Q96FH0	Protein MEF2BNB	1	2	-0.60	0.32	0.93			
Q9Y316	Protein MEMO1	2	6	0.01	0.24	0.23			
Q9H081	Protein MIS12 homolog	1	1	-0.12	-0.66	-0.55			
Q9Y2Z2	Protein MTO1 homolog, mitochondrial	1	1	1.18	0.47	-0.70			
Q92597	Protein NDRG1	10	92	0.61	0.53	-0.06	5	4	
Q9UN36	Protein NDRG2	2	5	0.36	-0.14	-0.50			
Q9UGV2	Protein NDRG3	3	18	-0.12	-0.05	0.02			
Q8NHV4	Protein NEDD1	4	7	0.03	-0.27	-0.26			
Q9BZQ8	Protein Niban	9	37	0.92	1.36	0.53	4	4	
Q9BPW8	Protein NipSnap homolog 1	7	55	0.29	-0.19	-0.42			
O75323	Protein NipSnap homolog 2	4	27	0.02	-0.11	-0.07			
Q7RTR2	Protein NLRC3	5	10	-0.09	0.07	0.23			
Q14207	Protein NPAT	1	1	0.10	0.41	0.32			
Q9H7Z3	Protein NRDE2 homolog	1	2	0.32	-0.40	-0.72			
Q96AB6	Protein N-terminal asparagine amidohydrolase	2	6	-0.36	-0.19	0.16			

P49757	Protein numb homolog	2	6	-0.04	0.12	0.13			
Q8NBL1	Protein O-glucosyltransferase 1	1	2	-0.44	-0.36	0.08			
Q86TB9	Protein PAT1 homolog 1	4	5	0.04	0.16	0.10			
Q9BVG4	Protein PBDC1	6	22	0.05	-0.12	-0.20			
Q9BRX2	Protein pelota homolog	2	2	0.19	0.01	-0.18			
Q96T49	Protein phosphatase 1 regulatory inhibitor subunit 16B	2	2	-0.19	0.20	0.40			
O14974	Protein phosphatase 1 regulatory subunit 12A	27	110	-0.28	0.08	0.41			
O60237	Protein phosphatase 1 regulatory subunit 12B	1	2	0.16	-0.13	-0.29			
Q9BZL4	Protein phosphatase 1 regulatory subunit 12C	15	41	-0.04	0.16	0.13			
Q96A00	Protein phosphatase 1 regulatory subunit 14A	1	2	-0.18	-2.60	-2.42			
Q96C90	Protein phosphatase 1 regulatory subunit 14B	1	2	0.12	0.56	0.45			
Q6ZM10	Protein phosphatase 1 regulatory subunit 21	10	24	-0.05	-0.21	-0.14			
O95685	Protein phosphatase 1 regulatory subunit 3D	1	1	-1.30	0.03	1.35			
Q9H7J1	Protein phosphatase 1 regulatory subunit 3E	3	3	-0.18	-0.41	-0.19			
Q15435	Protein phosphatase 1 regulatory subunit 7	16	83	0.00	-0.13	0.04			
P35813	Protein phosphatase 1A	9	42	-0.47	0.03	0.31			
O75688	Protein phosphatase 1B	10	77	-0.01	-0.07	-0.05			
P49593	Protein phosphatase 1F	5	23	-0.24	-0.25	0.04			
O15355	Protein phosphatase 1G	19	86	-0.19	-0.11	0.08			
Q8N3J5	Protein phosphatase 1K, mitochondrial	1	1	0.48	0.44	-0.03			
P41236	Protein phosphatase inhibitor 2	11	101	-0.04	-0.49	-0.50			5
Q9Y570	Protein phosphatase methyltransferase 1	6	16	-0.10	-0.15	-0.11			
Q8NI37	Protein phosphatase PTC7 homolog	3	11	-0.14	-0.19	0.00			
Q8WYL5	Protein phosphatase Slingshot homolog 1	1	2	0.21	-0.08	-0.28			
Q76176	Protein phosphatase Slingshot homolog 2	2	2	0.08	0.21	0.14			
Q8TE77	Protein phosphatase Slingshot homolog 3	1	1	-0.51	-0.29	0.20			
P29590	Protein PML	25	101	-0.37	-0.18	0.17			
Q8WVV4	Protein POF1B	1	2	3.00	2.60	-0.39			
Q86U86	Protein polybromo-1	15	29	-0.50	-0.15	0.32			
Q96M27	Protein PRRC1	8	40	0.22	-0.01	-0.16			
P48634	Protein PRRC2A	13	42	-0.04	-0.07	0.13			
Q5JSZ5	Protein PRRC2B	4	4	-0.25	-0.03	0.10			
Q9Y520	Protein PRRC2C	25	72	-0.10	-0.13	-0.02			
Q86TP1	Protein prune homolog	2	3	-0.11	-0.49	-0.49			
Q5XKP0	Protein QIL1	2	5	0.22	-0.06	-0.28			
Q96PU8	Protein quaking	8	71	-0.43	0.17	0.61			5
Q9P258	Protein RCC2	16	71	-0.21	-0.36	-0.14			5
Q13123	Protein Red	12	73	-0.20	-0.26	-0.12			
Q14690	Protein RRP5 homolog	17	53	0.49	-0.14	-0.67			5
Q9BY42	Protein RTF2 homolog	4	15	-0.03	-0.33	-0.25			
Q7L099	Protein RUFY3	1	2	NA	NA	NA			
P60903	Protein S100-A10	2	11	0.92	1.30	0.25	3		5
P31949	Protein S100-A11	6	107	0.62	0.77	0.64			5
P80511	Protein S100-A12	1	3	0.49	0.25	-0.13			
Q9HCY8	Protein S100-A14	1	1	NA	5.01	NA			
P26447	Protein S100-A4	8	305	1.06	1.43	0.42	4		5
P33763	Protein S100-A5	1	2	-0.34	-0.43	-0.08			
P06703	Protein S100-A6	7	80	1.18	0.45	-0.54	4		4
P31151	Protein S100-A7	2	32	0.00	-0.09	-0.09			
P05109	Protein S100-A8	6	81	0.73	0.00	-1.00	3		3
P06702	Protein S100-A9	8	100	0.34	0.14	-0.15			
P04271	Protein S100-B	1	13	0.20	-0.92	-1.26			4
P25815	Protein S100-P	1	1	2.68	2.19	-0.48			5
Q96ER3	Protein SAAL1	1	1	-0.23	-0.05	0.19			
Q99590	Protein SCAF11	13	23	-0.12	0.00	0.07			
Q9UPN6	Protein SCAF8	4	7	-0.85	-0.35	0.49			
O75880	Protein SCO1 homolog, mitochondrial	2	8	0.41	0.05	-0.33			
O43819	Protein SCO2 homolog, mitochondrial	3	4	-0.01	-0.20	-0.19			
Q14160	Protein scribble homolog	10	14	-0.17	0.23	0.41			
Q9NVU7	Protein SDA1 homolog	5	6	0.28	0.06	-0.21			
Q6IQ49	Protein SDE2 homolog	6	13	-0.14	-0.27	-0.12			
P55735	Protein SEC13 homolog	4	15	-0.46	0.10	0.59			
Q9UBV2	Protein sel-1 homolog 1	2	3	-0.18	0.22	0.40			
Q01105	Protein SET	12	78	0.04	-0.10	-0.13			
Q8ND04	Protein SMG8	3	10	-0.12	0.19	0.28			
Q9H0W8	Protein SMG9	2	3	-0.20	-0.19	0.01			
P18583	Protein SON	34	127	-0.18	-0.11	0.02			
Q68D10	Protein SPT2 homolog	3	7	0.04	0.21	0.22			
Q15532	Protein SSXT	2	4	0.05	0.12	0.07			
A3KN83	Protein strawberry notch homolog 1	4	15	0.39	-0.07	-0.39			
Q9Y2G9	Protein strawberry notch homolog 2	1	8	NA	NA	NA			
Q9BRJ7	Protein syndesmos	1	2	0.11	0.16	0.04			
Q5T011	Protein SZT2	1	2	NA	NA	NA			
Q969Z0	Protein TBRG4	3	3	0.19	0.13	-0.07			
Q92734	Protein TFG	6	19	0.18	0.35	0.22			
Q8WUY1	Protein THEM6	2	4	0.35	0.29	-0.10			
Q8N1K5	Protein THEMIS	11	24	0.97	-0.69	-1.65	5		4
Q5TEJ8	Protein THEMIS2	8	19	-0.22	0.29	0.52			
O15027	Protein transport protein Sec16A	18	59	-0.13	0.12	0.20			
Q15436	Protein transport protein Sec23A	8	54	0.12	0.29	0.25			
Q15437	Protein transport protein Sec23B	2	10	0.23	0.65	0.54			4
O95486	Protein transport protein Sec24A	1	4	NA	NA	NA			
O95487	Protein transport protein Sec24B	4	12	-0.04	0.06	-0.07			
P53992	Protein transport protein Sec24C	15	76	0.21	0.53	0.31			5
O94855	Protein transport protein Sec24D	1	3	-0.14	0.61	0.75			
O94979	Protein transport protein Sec31A	19	59	0.03	0.05	0.15			

P61619	Protein transport protein Sec61 subunit alpha isoform 1	2	6	0.74	0.87	0.11		3	
P60468	Protein transport protein Sec61 subunit beta	3	40	0.03	0.87	0.59		5	4
Q53HC9	Protein TSSC1	2	9	0.02	0.13	0.08			
Q9Y5U2	Protein TSSC4	4	15	0.01	0.14	0.11			
Q14761	Protein tyrosine phosphatase receptor type C-associated protein	4	14	0.77	0.33	-0.29	3		
Q12974	Protein tyrosine phosphatase type IVA 2	1	1	NA	NA	NA			
A6NIH7	Protein unc-119 homolog B	3	7	0.38	-0.03	-0.45			
Q8NB66	Protein unc-13 homolog C	1	1	-3.23	-1.11	2.12			
Q70J99	Protein unc-13 homolog D	11	46	0.09	0.24	0.28			
Q9H3U1	Protein unc-45 homolog A	15	38	0.04	0.23	0.19			
Q08AM6	Protein VAC14 homolog	3	16	0.14	0.19	-0.02			
Q69YN4	Protein virilizer homolog	1	4	0.05	0.25	0.10			
Q9Y4B6	Protein VPRBP	6	14	0.19	0.13	-0.05			
O95785	Protein Wiz	6	20	-0.12	-0.17	0.06			
O75695	Protein XRP2	2	5	-0.19	0.33	0.52			
Q5BJH7	Protein YIF1B	1	1	-0.16	0.16	0.32			
Q9GZM5	Protein YIPF3	1	1	-0.40	-0.31	0.10			
Q969M3	Protein YIPF5	1	8	0.09	0.25	0.09			
P62699	Protein yippee-like 5	2	5	-0.24	0.02	0.27			
Q08188	Protein-glutamine gamma-glutamyltransferase E	1	1	0.79	0.77	-0.01			
P22735	Protein-glutamine gamma-glutamyltransferase K	2	4	2.93	2.24	-0.68			
P22061	Protein-L-isoaspartate(D-aspartate) O-methyltransferase	14	84	-0.11	-0.30	-0.38			
Q8TDZ2	Protein-methionine sulfoxide oxidase MICAL1	9	17	-0.09	-0.12	-0.01			
Q7RTP6	Protein-methionine sulfoxide oxidase MICAL3	2	5	-0.67	-0.14	0.54			
Q14289	Protein-tyrosine kinase 2-beta	19	65	-0.46	0.17	0.54			4
O60704	Protein-tyrosine sulfotransferase 2	1	1	-0.53	-0.12	0.41			
Q04941	Proteolipid protein 2	1	4	1.55	0.76	-0.86	4	3	4
P06454	Prothymosin alpha	7	211	0.11	-0.52	-0.67			3
Q04864	Proto-oncogene c-Rel	8	23	-0.89	0.16	1.23	5		5
P12931	Proto-oncogene tyrosine-protein kinase Src	2	12	-0.46	0.16	0.62			
P15498	Proto-oncogene vav	10	23	-0.17	0.06	0.10			
P50336	Protoporphyrinogen oxidase	4	6	-0.40	0.21	0.64			
Q14242	P-selectin glycoprotein ligand 1	1	1	-0.55	-0.29	0.27			
Q08623	Pseudouridine-5'-monophosphatase	5	21	0.45	-0.09	-0.52			
Q96PZ0	Pseudouridylate synthase 7 homolog	3	3	0.28	0.01	-0.27			
P61457	Pterin-4-alpha-carbinolamine dehydratase	1	1	0.54	1.13	0.61			
Q9H0N5	Pterin-4-alpha-carbinolamine dehydratase 2	1	3	0.20	0.19	-0.03			
Q15397	Pumilio domain-containing protein KIAA0020	2	5	0.26	-0.11	-0.68			
Q14671	Pumilio homolog 1	3	16	-0.18	0.06	0.16			
Q8TB72	Pumilio homolog 2	3	14	-0.14	-0.27	-0.13			
P00491	Purine nucleoside phosphorylase	15	136	0.82	0.41	-0.26	4	4	
P55786	Puromycin-sensitive aminopeptidase	24	94	0.11	-0.09	-0.29			
O43865	Putative adenosylhomocysteinase 2	9	43	0.23	0.28	0.04			
Q96HN2	Putative adenosylhomocysteinase 3	6	39	0.08	-0.11	-0.11			
Q16740	Putative ATP-dependent Clp protease proteolytic subunit, mitochondrial	4	11	-0.14	-0.01	0.15			
Q7L2E3	Putative ATP-dependent RNA helicase DHX30	10	29	0.12	-0.22	-0.32			
Q5T1J5	Putative coiled-coil-helix-coiled-coil-helix domain-containing protein CHCHD	2	14	0.08	0.13	0.03			
Q6ZU45	Putative C-type lectin domain-containing protein LINC00083	1	1	1.65	0.85	-0.80			
Q6P1N9	Putative deoxyribonuclease TATDN1	4	10	0.29	0.06	-0.35			
Q9Y315	Putative deoxyribose-phosphate aldolase	5	19	-0.27	-0.02	0.23			
Q8N806	Putative E3 ubiquitin-protein ligase UBR7	3	6	-0.07	-0.13	0.03			
A6NKF9	Putative Golgi pH regulator C	2	2	-0.13	0.19	0.32			
Q9GZT8	Putative GTP cyclohydrolase 1 type 2 NIF3L1	7	15	0.23	-0.14	-0.44			
O43824	Putative GTP-binding protein 6	3	8	0.10	-0.10	-0.28			
Q58FF6	Putative heat shock protein HSP 90-beta 4	1	76	0.03	-0.39	-0.41			
Q9HCE1	Putative helicase MOV-10	5	10	0.12	0.11	-0.04			
O75884	Putative hydrolase RBBP9	2	3	0.21	0.28	0.08			
Q5T013	Putative hydroxypyruvate isomerase	1	1	0.43	0.00	-0.45			
A6NK58	Putative lipoyltransferase 2, mitochondrial	1	2	0.53	-0.63	-1.16			
Q96P11	Putative methyltransferase NSUN5	6	10	0.01	-0.24	-0.29			
Q96A73	Putative monooxygenase p33MONOX	4	7	0.09	-0.14	-0.14			
Q9Y303	Putative N-acetylglucosamine-6-phosphate deacetylase	4	6	0.09	0.27	0.01			
Q9BZK3	Putative nascent polypeptide-associated complex subunit alpha-like protein	1	28	0.26	-0.01	-0.34			
A8MVU1	Putative neutrophil cytosol factor 1C	1	1	-0.42	-0.04	0.38			
Q49A26	Putative oxidoreductase GLYR1	13	84	0.03	-0.09	-0.02			
Q6GMV3	Putative peptidyl-tRNA hydrolase PTRHD1	3	6	-1.03	-0.51	0.53			
Q8NHP8	Putative phospholipase B-like 2	5	10	0.25	0.68	0.34		4	
O43143	Putative pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15	30	188	0.01	-0.14	-0.04			
O60231	Putative pre-mRNA-splicing factor ATP-dependent RNA helicase DHX16	7	30	-0.07	0.05	0.32			
Q6P2P2	Putative protein arginine N-methyltransferase 10	2	2	-0.01	-0.22	-0.22			
Q6ZMU1	Putative protein C3P1	1	1	NA	NA	NA			
P58557	Putative ribonuclease	1	1	-0.55	-0.20	0.36			
P46087	Putative ribosomal RNA methyltransferase NOP2	16	74	0.33	-0.23	-0.48			
Q8N0V3	Putative ribosome-binding factor A, mitochondrial	1	1	0.01	-0.56	-0.59			
Q8XW55	Putative RNA polymerase II subunit B1 CTD phosphatase RPAP2	3	5	0.05	0.22	0.13			
Q96T37	Putative RNA-binding protein 15	15	62	-0.34	-0.26	0.05			
Q8NDT2	Putative RNA-binding protein 15B	4	11	0.01	0.06	0.09			
P98179	Putative RNA-binding protein 3	3	29	-0.02	-0.11	0.01			
Q9NQ29	Putative RNA-binding protein Luc7-like 1	1	48	0.23	-0.13	-0.43			
Q9Y383	Putative RNA-binding protein Luc7-like 2	11	164	-0.12	-0.20	-0.12			
P0C7V7	Putative signal peptidase complex catalytic subunit SEC11B	1	2	-0.86	-0.29	0.57			
Q9HBR0	Putative sodium-coupled neutral amino acid transporter 10	1	2	-0.51	-0.11	0.40			
Q5T440	Putative transferase CAF17, mitochondrial	5	14	0.36	0.07	-0.31			
A6NL28	Putative tropomyosin alpha-3 chain-like protein	4	82	-0.38	-0.15	0.26			
I3L1I5	Putative uncharacterized protein LOC100996504	1	3	0.05	-0.73	-0.77			
C4AMC7	Putative WAS protein family homolog 3	1	14	-0.12	-0.10	0.02			

Q9BRQ0	Pygopus homolog 2	1	2	-0.36	-0.13	0.23			
Q8WU10	Pyridine nucleotide-disulfide oxidoreductase domain-containing protein 1	1	1	-0.01	0.14	0.15			
O00764	Pyridoxal kinase	10	23	0.43	0.28	-0.42			
Q96GD0	Pyridoxal phosphate phosphatase	4	18	-0.65	-0.18	0.52	4		
Q6P996	Pyridoxal-dependent decarboxylase domain-containing protein 1	3	5	-0.53	0.25	0.69			3
Q9NVS9	Pyridoxine-5'-phosphate oxidase	2	2	0.82	0.55	-0.26			
Q6K0P9	Pyrim and HIN domain-containing protein 1	13	85	-0.16	0.70	0.95		5	5
Q96C36	Pyrraline-5-carboxylate reductase 2	4	7	0.25	-0.29	-0.53			
Q53H96	Pyrraline-5-carboxylate reductase 3	4	7	0.07	0.06	0.01			
P08559	Pyruvate dehydrogenase E1 component subunit alpha, somatic form, mitoc	12	63	0.35	0.03	-0.33			
P11177	Pyruvate dehydrogenase E1 component subunit beta, mitochondrial	13	134	0.30	-0.01	-0.29			
Q8NCN5	Pyruvate dehydrogenase phosphatase regulatory subunit, mitochondrial	7	15	0.26	0.22	-0.14			
O00330	Pyruvate dehydrogenase protein X component, mitochondrial	11	30	0.03	-0.12	-0.01			
P14618	Pyruvate kinase PKM	41	624	0.57	-0.10	-0.65	5		5
Q9BXR0	Queuine tRNA-ribosyltransferase	2	4	NA	NA	NA			
Q08257	Quinone oxidoreductase	17	78	-0.03	-0.07	-0.02			
O95825	Quinone oxidoreductase-like protein 1	1	6	-0.01	-0.26	-0.20			
Q9Y3T6	R3H and coiled-coil domain-containing protein 1	1	1	0.29	0.00	-0.30			
Q15032	R3H domain-containing protein 1	2	4	-0.75	-0.58	0.25	3		4
Q9Y2K5	R3H domain-containing protein 2	2	2	-0.81	-0.19	0.63			
P31150	Rab GDP dissociation inhibitor alpha	16	118	0.60	0.65	-0.22	5		5
P50395	Rab GDP dissociation inhibitor beta	12	168	0.21	0.33	0.03			
Q9Y3P9	Rab GTPase-activating protein 1	6	13	0.24	0.15	0.00			
Q5R372	Rab GTPase-activating protein 1-like	5	17	-0.18	0.26	0.35			
Q15276	Rab GTPase-binding effector protein 1	13	24	-0.03	0.01	-0.07			
Q9H5N1	Rab GTPase-binding effector protein 2	11	31	-0.52	0.00	0.48	5		
Q6WKZ4	Rab11 family-interacting protein 1	7	12	-0.69	0.52	1.08			4
Q6BDI9	Rab15 effector protein	1	1	-1.05	0.79	1.85			
Q15042	Rab3 GTPase-activating protein catalytic subunit	5	9	0.25	-0.37	-0.63			4
Q9H2M9	Rab3 GTPase-activating protein non-catalytic subunit	6	25	0.13	-0.19	-0.40			
Q9UJ41	Rab5 GDP/GTP exchange factor	2	2	-0.23	0.02	0.25			
Q7Z6M1	Rab9 effector protein with kelch motifs	1	1	-0.26	-0.66	-0.42			
Q9H1K0	Rabenosyn-5	1	1	0.14	0.20	0.06			
Q9UBK7	Rab-like protein 2A	1	4	-0.12	-0.04	0.08			
Q5HYI8	Rab-like protein 3	4	13	0.07	-0.08	-0.07			
Q3YEC7	Rab-like protein 6	6	11	-0.10	0.21	0.25			
P31749	RAC-alpha serine/threonine-protein kinase	4	16	-0.15	0.21	0.32			
P31751	RAC-beta serine/threonine-protein kinase	2	10	-0.10	0.03	-0.14			
Q9HA92	Radical S-adenosyl methionine domain-containing protein 1, mitochondrial	2	2	-0.15	-0.09	0.06			
P35241	Radixin	5	404	-0.02	0.40	0.63			3
P04049	RAF proto-oncogene serine/threonine-protein kinase	2	7	0.00	0.30	0.30			
Q14699	Raftlin	7	28	-0.46	0.11	0.72			3
Q6IAA8	Regulator complex protein LAMTOR1	6	22	-0.12	-0.04	0.09			
Q9Y2Q5	Regulator complex protein LAMTOR2	2	8	-0.11	0.00	0.12			
Q9UHA4	Regulator complex protein LAMTOR3	1	5	0.25	0.45	0.21			
O43504	Regulator complex protein LAMTOR5	1	11	-0.44	-0.33	0.25	5		
Q6GYQ0	Ral GTPase-activating protein subunit alpha-1	2	5	-0.57	-0.05	0.52			
Q2PPJ7	Ral GTPase-activating protein subunit alpha-2	2	11	0.09	0.34	0.24			
Q86X10	Ral GTPase-activating protein subunit beta	2	8	0.20	0.30	0.10			
Q15311	RalA-binding protein 1	5	8	0.03	0.20	-0.08			
Q96D71	RalBP1-associated Eps domain-containing protein 1	10	26	-0.03	-0.15	0.06			
P46060	Ran GTPase-activating protein 1	20	90	0.00	0.16	0.04			
Q9HD47	Ran guanine nucleotide release factor	1	1	0.39	0.04	-0.34			
Q6VN20	Ran-binding protein 10	2	4	-0.44	-0.15	0.30			
Q9H6Z4	Ran-binding protein 3	8	37	-0.05	-0.19	-0.15			
Q96S59	Ran-binding protein 9	3	4	0.16	0.43	0.28			
Q9BYM8	RanBP-type and C3HC4-type zinc finger-containing protein 1	7	21	0.01	0.05	0.04			
P43487	Ran-specific GTPase-activating protein	6	34	-0.02	-0.08	-0.23			
Q13905	Rap guanine nucleotide exchange factor 1	7	15	-0.06	0.05	0.46			
Q8TEU7	Rap guanine nucleotide exchange factor 6	8	20	0.09	-0.20	-0.26			
Q684P5	Rap1 GTPase-activating protein 2	15	40	-1.14	0.35	1.40	4		4
P52306	Rap1 GTPase-GDP dissociation stimulator 1	8	22	0.02	0.24	0.27			
Q6R327	Rapamycin-insensitive companion of mTOR	2	2	-0.18	0.24	0.41			
Q8TB24	Ras and Rab interactor 3	6	15	-0.88	-0.54	0.26	4		
Q9NS23	Ras association domain-containing protein 1	2	3	-0.50	0.49	0.99			
P50749	Ras association domain-containing protein 2	10	50	0.86	0.31	-0.85	5		3
Q9H2L5	Ras association domain-containing protein 4	1	10	-1.63	-0.13	1.51	4		4
Q8WWW0	Ras association domain-containing protein 5	5	15	-0.28	-0.09	0.49			
P20936	Ras GTPase-activating protein 1	1	2	0.31	0.02	-0.28			
Q15283	Ras GTPase-activating protein 2	2	80	0.13	-0.27	-0.26			
Q14644	Ras GTPase-activating protein 3	16	37	-0.14	-0.24	0.08			
Q13283	Ras GTPase-activating protein-binding protein 1	10	59	0.02	0.09	0.19			
Q9UN86	Ras GTPase-activating protein-binding protein 2	3	9	0.38	0.21	-0.74			
P46940	Ras GTPase-activating-like protein IQGAP1	75	675	-0.31	0.51	0.85		4	3
Q13576	Ras GTPase-activating-like protein IQGAP2	38	192	-0.30	0.41	0.68			3
O95267	RAS guanyl-releasing protein 1	1	1	0.59	0.56	-0.02			
Q7LDG7	RAS guanyl-releasing protein 2	6	26	-0.19	-0.24	0.09			
Q86YV0	RAS protein activator like-3	33	200	0.05	0.19	0.29			
Q15404	Ras suppressor protein 1	8	38	0.03	0.27	0.25			
P63000	Ras-related C3 botulinum toxin substrate 1	5	64	0.31	0.38	-0.30			
P15153	Ras-related C3 botulinum toxin substrate 2	7	213	0.05	-0.29	-0.22			
Q7L523	Ras-related GTP-binding protein A	1	3	-0.20	0.11	0.24			
Q9HB90	Ras-related GTP-binding protein C	4	5	0.33	0.29	-0.03			
P61026	Ras-related protein Rab-10	5	79	0.23	0.25	-0.04			
Q15907	Ras-related protein Rab-11B	10	82	-0.12	0.11	0.19			
P61106	Ras-related protein Rab-14	10	66	-0.05	0.22	0.10			

Q9NP72	Ras-related protein Rab-18	6	18	0.73	0.63	0.17	5	5
P62820	Ras-related protein Rab-1A	6	138	0.14	0.13	0.05		
Q9H0U4	Ras-related protein Rab-1B	7	172	-0.17	0.07	0.36		
Q9UL25	Ras-related protein Rab-21	4	20	0.00	0.19	0.23		
Q9UL26	Ras-related protein Rab-22A	2	3	0.24	0.41	0.16		
Q969Q5	Ras-related protein Rab-24	1	2	-0.36	-0.17	0.20		
P51159	Ras-related protein Rab-27A	2	10	0.09	0.83	0.77	4	3
O00194	Ras-related protein Rab-27B	1	1	-0.12	-0.09	0.03		
P51157	Ras-related protein Rab-28	2	2	0.23	-0.03	-0.26		
P61019	Ras-related protein Rab-2A	2	19	0.12	0.33	0.21		
Q8WUD1	Ras-related protein Rab-2B	1	14	-0.36	0.06	0.42		
Q9H082	Ras-related protein Rab-33B	1	11	0.45	0.55	0.11		
Q15286	Ras-related protein Rab-35	3	73	0.21	0.42	0.20		
Q96AX2	Ras-related protein Rab-37	3	10	-0.57	0.00	0.63		
Q96DA2	Ras-related protein Rab-39B	2	10	0.11	-0.02	-0.15		
O95716	Ras-related protein Rab-3D	1	15	0.32	0.60	0.29		
Q96S21	Ras-related protein Rab-40C	1	8	1.24	0.96	-0.28		
Q86Y56	Ras-related protein Rab-43	1	6	0.06	-0.50	-0.55		
P61018	Ras-related protein Rab-4B	3	17	-0.43	0.13	0.61		
P20339	Ras-related protein Rab-5A	4	29	0.02	0.40	0.29		
P61020	Ras-related protein Rab-5B	5	84	-0.08	0.06	0.27		
P51148	Ras-related protein Rab-5C	8	81	-0.20	0.17	0.36		
P20340	Ras-related protein Rab-6A	4	58	0.22	0.52	0.43	5	
Q9NRW1	Ras-related protein Rab-6B	1	24	2.08	1.69	-0.39		
Q9H0N0	Ras-related protein Rab-6C	1	2	0.12	0.42	0.30		
P51149	Ras-related protein Rab-7a	13	103	0.11	0.11	0.04		
O14966	Ras-related protein Rab-7L1	3	13	-0.23	0.59	0.97	5	4
P61006	Ras-related protein Rab-8A	5	130	-0.16	0.27	0.48		
Q92930	Ras-related protein Rab-8B	6	177	-0.29	0.34	0.64		3
P51151	Ras-related protein Rab-9A	2	11	0.17	0.76	0.47	5	
P11233	Ras-related protein Ral-A	3	16	0.34	-0.05	-0.44		
P11234	Ras-related protein Ral-B	3	11	-0.28	0.06	0.34		
P62834	Ras-related protein Rap-1A	1	107	0.35	0.04	-0.06		
P61224	Ras-related protein Rap-1b	2	128	-0.44	-0.03	0.41		
P61225	Ras-related protein Rap-2b	7	32	-0.33	0.33	0.50		
P62070	Ras-related protein R-Ras2	5	41	0.17	0.71	0.62	5	4
Q00765	Receptor expression-enhancing protein 5	6	26	0.48	0.78	0.13	5	5
O00559	Receptor-binding cancer antigen expressed on SiSo cells	1	1	0.18	-0.26	-0.46		
Q13546	Receptor-interacting serine/threonine-protein kinase 1	6	16	-0.10	0.05	0.25		
O43353	Receptor-interacting serine/threonine-protein kinase 2	1	1	-0.60	-0.30	0.31		
Q9Y572	Receptor-interacting serine/threonine-protein kinase 3	1	3	-0.78	-0.36	0.40		
P18433	Receptor-type tyrosine-protein phosphatase alpha	1	13	-0.49	0.63	1.13		
P08575	Receptor-type tyrosine-protein phosphatase C	38	379	0.21	0.40	0.26		
P23469	Receptor-type tyrosine-protein phosphatase epsilon	1	3	-0.23	0.19	0.43		
Q12913	Receptor-type tyrosine-protein phosphatase eta	9	19	-0.25	0.33	0.72		5
Q06330	Recombining binding protein suppressor of hairless	6	8	0.23	0.24	-0.13		
Q15493	Regucalcin	1	3	1.94	2.23	0.30		
Q96P16	Regulation of nuclear pre-mRNA domain-containing protein 1A	1	7	0.07	0.13	0.13		
Q9NQG5	Regulation of nuclear pre-mRNA domain-containing protein 1B	8	46	-0.19	-0.15	-0.13		
Q5VT52	Regulation of nuclear pre-mRNA domain-containing protein 2	14	36	-0.05	-0.10	-0.08		
Q9H4X1	Regulator of cell cycle RGCC	1	3	-2.62	-1.53	1.10		
P18754	Regulator of chromosome condensation	11	65	0.12	0.18	-0.02		
O43665	Regulator of G-protein signaling 10	11	108	0.39	-1.42	-1.68	5	5
O43566	Regulator of G-protein signaling 14	10	42	0.34	0.17	-0.11		
Q9NS28	Regulator of G-protein signaling 18	1	1	0.30	0.27	-0.05		
P49795	Regulator of G-protein signaling 19	3	9	0.59	1.06	0.44		3
P49796	Regulator of G-protein signaling 3	11	59	-0.90	0.41	1.30	5	5
Q96DB5	Regulator of microtubule dynamics protein 1	6	30	-0.03	0.14	0.13		
Q96TC7	Regulator of microtubule dynamics protein 3	2	15	-0.77	0.44	1.21	4	5
Q92900	Regulator of nonsense transcripts 1	27	116	0.09	0.09	0.03		
Q9HAU5	Regulator of nonsense transcripts 2	7	30	0.00	-0.16	-0.12		
Q9H1J1	Regulator of nonsense transcripts 3A	3	4	-0.10	-0.57	-0.52		
Q9BZ17	Regulator of nonsense transcripts 3B	4	6	0.23	0.06	-0.04		
O00287	Regulatory factor X-associated protein	1	1	-1.49	-0.56	0.95		
Q8N122	Regulatory-associated protein of mTOR	1	1	0.13	0.05	-0.10		
Q96T23	Remodeling and spacing factor 1	10	17	-0.03	0.05	0.02		
P35251	Replication factor C subunit 1	11	30	0.04	-0.08	-0.18		
P35250	Replication factor C subunit 2	3	9	-0.05	-0.06	0.00		
P40938	Replication factor C subunit 3	3	11	-0.08	-0.18	-0.05		
P35249	Replication factor C subunit 4	14	28	-0.10	-0.19	-0.06		
P40937	Replication factor C subunit 5	1	2	0.49	0.21	-0.27		
Q9BWE0	Replication initiator 1	1	4	-1.18	-0.33	1.12		
P35244	Replication protein A 14 kDa subunit	3	19	-0.06	-0.11	-0.16		
P15927	Replication protein A 32 kDa subunit	8	59	0.20	-0.06	-0.13		
P27694	Replication protein A 70 kDa DNA-binding subunit	25	189	-0.12	-0.11	-0.09		
Q9H063	Repressor of RNA polymerase III transcription MAF1 homolog	1	1	-0.18	0.01	0.20		
Q9UKL0	REST corepressor 1	2	2	0.00	-0.04	-0.04		
Q9P2K3	REST corepressor 3	1	2	-1.47	-0.65	0.83		
Q15293	Reticulocalbin-1	1	1	-0.09	0.67	0.74		
Q14257	Reticulocalbin-2	5	8	0.25	-0.22	-0.39		
Q96D15	Reticulocalbin-3	1	1	0.24	0.43	0.19		
Q9NQC3	Reticulon-4	3	20	-0.40	-0.29	0.46		
Q8WWV3	Reticulon-4-interacting protein 1, mitochondrial	2	5	-0.05	-0.29	-0.23		
O43924	Retinal rod rhodopsin-sensitive cGMP 3',5'-cyclic phosphodiesterase subunit	1	2	0.04	0.26	0.21		
Q15291	Retinoblastoma-binding protein 5	10	28	-0.04	-0.07	-0.11		
Q08999	Retinoblastoma-like protein 2	4	7	-0.42	-0.34	0.09		

P28702	Retinoic acid receptor RXR-beta	2	4	0.23	-0.06	-0.20			
Q7Z5J4	Retinoic acid-induced protein 1	2	3	-0.25	-0.15	0.08			
Q9HB40	Retinoid-inducible serine carboxypeptidase	3	9	-0.33	-0.14	0.13			
Q8TC12	Retinol dehydrogenase 11	3	12	0.04	0.13	0.22			
Q8NBN7	Retinol dehydrogenase 13	10	31	-0.07	0.02	-0.07			
Q9HBH5	Retinol dehydrogenase 14	7	21	-0.12	0.00	0.11			
O95980	Reversion-inducing cysteine-rich protein with Kazal motifs	1	1	-0.02	-0.03	-0.01			
P52565	Rho GDP-dissociation inhibitor 1	11	135	0.29	0.22	-0.07			
P52566	Rho GDP-dissociation inhibitor 2	15	228	0.13	-0.33	-0.50			4
Q07960	Rho GTPase-activating protein 1	10	36	-0.25	0.32	0.72			3
Q53QZ3	Rho GTPase-activating protein 15	9	31	-0.08	-0.46	-0.42		5	
Q68EM7	Rho GTPase-activating protein 17	11	30	-0.32	-0.19	0.19			
Q8N392	Rho GTPase-activating protein 18	4	5	-0.38	0.18	0.64			
P42331	Rho GTPase-activating protein 25	27	172	-0.01	0.32	0.37			
Q9UNA1	Rho GTPase-activating protein 26	2	5	-0.09	0.22	0.44			
Q6ZUM4	Rho GTPase-activating protein 27	5	10	-0.63	0.08	0.72			
Q7Z6I6	Rho GTPase-activating protein 30	12	43	-0.45	-0.05	0.47			
Q9NRY4	Rho GTPase-activating protein 35	1	1	-0.03	0.27	0.31			
P98171	Rho GTPase-activating protein 4	22	86	0.06	-0.09	-0.09			
Q9BRR9	Rho GTPase-activating protein 9	10	33	-0.34	-0.18	0.15			
Q92888	Rho guanine nucleotide exchange factor 1	31	266	-0.17	-0.06	0.11			
Q9HCE6	Rho guanine nucleotide exchange factor 10-like protein	1	1	0.04	0.40	0.36			
Q6ZSZ5	Rho guanine nucleotide exchange factor 18	17	42	0.22	-0.26	-0.48			5
Q92974	Rho guanine nucleotide exchange factor 2	16	63	-0.27	-0.15	0.30			
Q15052	Rho guanine nucleotide exchange factor 6	10	44	0.12	0.04	0.02			
Q14155	Rho guanine nucleotide exchange factor 7	6	28	0.34	0.55	0.13			
Q13464	Rho-associated protein kinase 1	23	87	-0.18	-0.03	0.21			
O75116	Rho-associated protein kinase 2	4	46	-0.22	0.16	0.49			
Q8TEB9	Rhomboid-related protein 4	1	1	0.02	0.30	0.26			
P08134	Rho-related GTP-binding protein RhoC	1	71	-0.77	1.32	2.07		3	
Q9HBH0	Rho-related GTP-binding protein RhoF	3	8	0.12	0.36	0.35			
P84095	Rho-related GTP-binding protein RhoG	8	72	0.00	0.06	0.18			
Q15669	Rho-related GTP-binding protein RhoH	3	5	-0.10	-0.47	-0.35			
Q9H477	Ribokinase	1	3	0.37	-0.15	-0.21			
O75792	Ribonuclease H2 subunit A	6	13	0.03	-0.23	-0.28			
Q5TBB1	Ribonuclease H2 subunit B	4	10	-0.40	-0.34	-0.03			
Q8TDP1	Ribonuclease H2 subunit C	3	11	-0.14	-0.07	-0.05			
P13489	Ribonuclease inhibitor	13	95	0.20	0.04	-0.23			
O95059	Ribonuclease P protein subunit p14	1	3	NA	NA	NA			
O75817	Ribonuclease P protein subunit p20	1	3	-0.03	-0.18	-0.14			
Q9BUL9	Ribonuclease P protein subunit p25	2	10	0.13	-0.30	-0.32			
Q8N5L8	Ribonuclease P protein subunit p25-like protein	1	1	-0.43	-0.05	0.40			
O95707	Ribonuclease P protein subunit p29	2	3	0.72	0.40	-0.31			
P78346	Ribonuclease P protein subunit p30	3	4	0.36	-0.04	-0.26			
P78345	Ribonuclease P protein subunit p38	1	3	0.19	0.03	-0.16			
O75818	Ribonuclease P protein subunit p40	1	2	NA	NA	NA			
O00584	Ribonuclease T2	4	39	0.68	0.25	-0.27		5	
P52758	Ribonuclease UK114	4	9	0.02	-0.22	-0.24			
Q5D1E8	Ribonuclease ZC3H12A	1	1	0.05	-0.13	-0.17			
Q99575	Ribonucleases P/MRP protein subunit POP1	5	17	-0.08	-0.18	-0.13			
Q8IY67	Ribonucleoprotein PTB-binding 1	7	36	-0.05	-0.02	-0.06			
Q9HCJ3	Ribonucleoprotein PTB-binding 2	1	1	0.70	0.87	0.19			
P23921	Ribonucleoside-diphosphate reductase large subunit	1	1	0.50	0.31	-0.18			
Q7LG56	Ribonucleoside-diphosphate reductase subunit M2 B	1	1	0.03	0.17	0.15			
P49247	Ribose-5-phosphate isomerase	9	41	0.00	-0.65	-0.73		4	5
P60891	Ribose-phosphate pyrophosphokinase 1	5	77	0.37	0.01	-0.47			
P11908	Ribose-phosphate pyrophosphokinase 2	5	58	0.00	-0.35	-0.20			
Q9Y4W2	Ribosomal biogenesis protein LAS1L	4	7	0.05	-0.14	-0.18			
O76021	Ribosomal L1 domain-containing protein 1	17	102	0.51	-0.03	-0.47		5	5
Q9BQC6	Ribosomal protein 63, mitochondrial	2	9	0.14	-0.08	-0.06			
Q15418	Ribosomal protein S6 kinase alpha-1	7	51	-0.29	0.04	0.40			
P51812	Ribosomal protein S6 kinase alpha-3	21	186	0.72	0.44	-0.19		5	5
O75676	Ribosomal protein S6 kinase alpha-4	4	10	0.01	0.29	0.25			
O75582	Ribosomal protein S6 kinase alpha-5	5	6	0.10	0.22	0.25			
P23443	Ribosomal protein S6 kinase beta-1	2	3	0.04	-0.06	-0.08			
Q9UBS0	Ribosomal protein S6 kinase beta-2	1	4	-0.22	0.05	0.26			
Q9Y6S9	Ribosomal protein S6 kinase-like 1	1	1	-0.48	-0.42	0.07			
P56182	Ribosomal RNA processing protein 1 homolog A	7	21	0.46	-0.16	-0.73			3
Q14684	Ribosomal RNA processing protein 1 homolog B	16	42	0.22	-0.27	-0.49			4
Q96EU6	Ribosomal RNA processing protein 36 homolog	3	3	0.15	-0.15	-0.31			
Q92979	Ribosomal RNA small subunit methyltransferase NEP1	4	14	0.25	-0.23	-0.54			5
Q9Y3A4	Ribosomal RNA-processing protein 7 homolog A	2	4	0.45	-0.11	-0.56			
O43159	Ribosomal RNA-processing protein 8	5	8	-0.07	0.02	0.12			
O43709	Ribosome biogenesis methyltransferase WBSCR22	3	9	-0.08	-0.29	-0.15			
Q14692	Ribosome biogenesis protein BMS1 homolog	9	22	0.19	-0.04	-0.20			
Q14137	Ribosome biogenesis protein BOP1	7	16	0.19	0.04	-0.15			
Q8TDN6	Ribosome biogenesis protein BRX1 homolog	2	13	0.53	-0.14	-0.67			5
O95478	Ribosome biogenesis protein NSA2 homolog	1	1	0.59	-0.21	-0.82			
Q9GZL7	Ribosome biogenesis protein WDR12	5	10	0.20	-0.05	-0.28			
Q15050	Ribosome biogenesis regulatory protein homolog	7	25	0.61	0.18	-0.54		4	
Q9Y3A5	Ribosome maturation protein SBDS	7	25	0.39	-0.24	-0.63			3
Q9H9Y2	Ribosome production factor 1	2	2	0.34	-0.05	-0.38			
Q9H7B2	Ribosome production factor 2 homolog	1	6	1.30	0.50	-0.82			
Q9P2E9	Ribosome-binding protein 1	44	130	-0.43	0.36	0.86			5
Q96E11	Ribosome-recycling factor, mitochondrial	4	6	0.19	-0.21	-0.10			
Q969S9	Ribosome-releasing factor 2, mitochondrial	2	5	0.66	0.33	-0.33			

P16083	Ribosyl-dihydroxy-nicotinamide dehydrogenase	5	9	-0.09	0.04	0.23			
Q96AT9	Ribulose-phosphate 3-epimerase	3	10	-0.51	-0.16	0.44			
Q96PM5	RING finger and CHY zinc finger domain-containing protein 1	1	2	NA	NA	NA			
O15541	RING finger protein 113A	4	11	0.01	-0.07	0.08			
Q9Y508	RING finger protein 114	3	12	-0.16	-0.15	0.09			
Q9BXT8	RING finger protein 17	1	1	0.51	1.23	0.70			
Q8ND24	RING finger protein 214	4	6	0.09	-0.09	-0.03			
Q5W0B1	RING finger protein 219	1	1	-0.11	-0.16	-0.06			
Q9C0B0	RING finger protein unkempt homolog	4	13	0.06	-0.07	-0.10			
Q8N488	RING1 and YY1-binding protein	1	5	-0.29	-0.09	0.24			
O00442	RNA 3'-terminal phosphate cyclase	5	40	0.14	0.05	-0.11			
Q9Y2P8	RNA 3'-terminal phosphate cyclase-like protein	2	3	0.58	-0.21	-0.62			
Q96E39	RNA binding motif protein, X-linked-like-1	4	261	-0.01	-0.36	0.05			
Q6P6C2	RNA demethylase ALKBH5	8	22	-0.11	-0.25	-0.25			
Q9GZR2	RNA exonuclease 4	1	1	0.35	-0.46	-0.80			
Q9HC36	RNA methyltransferase-like protein 1	1	1	0.41	-0.03	-0.44			
P55199	RNA polymerase II elongation factor ELL	4	13	0.25	0.83	0.72			
Q9Y5B0	RNA polymerase II subunit A C-terminal domain phosphatase	8	15	-0.14	-0.11	-0.22			
Q9NP77	RNA polymerase II subunit A C-terminal domain phosphatase SSU72	3	4	0.07	-0.26	-0.33			
Q8N7H5	RNA polymerase II-associated factor 1 homolog	7	17	0.04	0.01	-0.05			
Q9BWH6	RNA polymerase II-associated protein 1	3	3	-0.25	-0.01	0.23			
Q9H6T3	RNA polymerase II-associated protein 3	7	24	-0.02	-0.27	-0.31			
Q6PD62	RNA polymerase-associated protein CTR9 homolog	7	16	-0.07	0.08	0.08			
Q8WVC0	RNA polymerase-associated protein LEO1	1	1	-0.16	0.32	0.46			
Q92541	RNA polymerase-associated protein RTF1 homolog	11	23	-0.10	-0.03	0.05			
Q8IZ73	RNA pseudouridylate synthase domain-containing protein 2	1	1	-0.16	-0.39	-0.23			
P38159	RNA-binding motif protein, X chromosome	9	362	-0.48	-0.45	0.23		5	
Q9Y388	RNA-binding motif protein, X-linked 2	1	1	-0.13	-0.20	-0.08			
P29558	RNA-binding motif, single-stranded-interacting protein 1	3	4	-0.20	0.47	0.70			
P98175	RNA-binding protein 10	18	50	-0.17	-0.11	0.07			
Q9NTZ6	RNA-binding protein 12	12	50	0.01	-0.08	-0.05			
Q8IXT5	RNA-binding protein 12B	3	4	-0.02	0.00	0.02			
Q96PK6	RNA-binding protein 14	19	184	-0.22	-0.17	0.02			
P49756	RNA-binding protein 25	15	63	-0.11	-0.25	-0.04			
Q5T8P6	RNA-binding protein 26	14	48	-0.06	-0.27	-0.19			
Q9P2N5	RNA-binding protein 27	6	28	-0.35	-0.15	0.21			
Q9NW13	RNA-binding protein 28	11	26	0.25	0.05	-0.18			
Q96EV2	RNA-binding protein 33	8	12	-0.35	-0.23	0.24			
P42696	RNA-binding protein 34	11	30	0.04	-0.25	-0.13			
Q9H0Z9	RNA-binding protein 38	3	6	-0.36	-0.08	0.27			
Q14498	RNA-binding protein 39	17	145	-0.18	-0.13	0.09			
Q9BWF3	RNA-binding protein 4	2	73	-0.22	-0.38	-0.06			
Q9BTD8	RNA-binding protein 42	4	13	-0.01	-0.22	-0.12			
Q8IUH3	RNA-binding protein 45	1	5	-0.33	-0.19	0.00			
Q9BQ04	RNA-binding protein 4B	2	56	-0.19	0.05	0.31			
P52756	RNA-binding protein 5	11	23	-0.07	-0.06	-0.01			
P78332	RNA-binding protein 6	8	10	-0.05	-0.07	-0.05			
Q9Y580	RNA-binding protein 7	3	13	-0.24	0.05	0.29			
Q9Y559	RNA-binding protein 8A	5	73	-0.17	-0.13	0.01			
Q01844	RNA-binding protein EWS	6	75	0.16	0.03	0.02			
P35637	RNA-binding protein FUS	9	91	-0.12	-0.27	-0.06			
Q96DH6	RNA-binding protein Musashi homolog 2	1	3	-0.14	-0.23	-0.09			
Q9ULX3	RNA-binding protein NOB1	1	2	-0.03	-0.41	-0.37			
Q9NRX1	RNA-binding protein PNO1	6	18	0.08	-0.26	-0.56			
Q9UKM9	RNA-binding protein Raly	18	177	-0.44	-0.10	0.40		5	
Q93062	RNA-binding protein with multiple splicing	1	2	NA	NA	NA			
Q15287	RNA-binding protein with serine-rich domain 1	6	39	-0.14	-0.11	0.05			
Q5TZA2	Rootletin	16	49	0.14	-0.06	-0.06			
Q5TC82	Roquin-1	1	1	-0.27	-0.14	0.13			
Q5VWQ0	Round spermatid basic protein 1	4	8	0.25	-0.21	-0.20			
Q6PCB5	Round spermatid basic protein 1-like protein	1	1	-0.04	-0.23	-0.20			
P22087	rRNA 2'-O-methyltransferase fibrillarin	20	284	0.49	0.04	-0.64		5	5
Q6IN84	rRNA methyltransferase 1, mitochondrial	1	2	0.44	-0.24	-0.68			
Q9Y324	rRNA-processing protein FCF1 homolog	1	1	0.24	-0.03	-0.27			
Q9BRU9	rRNA-processing protein UTP23 homolog	2	3	0.32	-0.38	-0.71			
Q5JTH9	RRP12-like protein	6	13	0.18	-0.22	-0.39			
Q9Y3B9	RRP15-like protein	1	4	0.52	-0.08	-0.74			3
Q96T51	RUN and FYVE domain-containing protein 1	9	35	-0.42	-0.22	0.21			
Q92622	Run domain Beclin-1 interacting and cysteine-rich containing protein	1	5	-0.62	0.17	0.78			
Q01196	Runt-related transcription factor 1	5	17	0.10	0.18	0.01			
Q13950	Runt-related transcription factor 2	3	15	0.70	0.79	-0.18			
Q13761	Runt-related transcription factor 3	5	50	-0.54	0.03	0.50			5
Q9Y265	RuvB-like 1	24	211	0.10	-0.13	-0.20			
Q9Y230	RuvB-like 2	22	193	0.13	-0.01	-0.17			
Q92736	Ryanodine receptor 2	1	2	-0.17	0.17	0.33			
Q8N5C6	S1 RNA-binding domain-containing protein 1	1	1	-1.11	-1.25	-0.12			
Q96BU1	S100P-binding protein	1	2	-0.02	0.11	0.13			
Q8NBX0	Saccharopine dehydrogenase-like oxidoreductase	4	19	0.05	-0.10	-0.15			
Q00266	S-adenosylmethionine synthase isoform type-1	1	2	0.59	0.79	0.21			
P31153	S-adenosylmethionine synthase isoform type-2	11	92	-0.02	0.06	0.00			
Q9NWH9	SAFB-like transcription modulator	18	48	-0.10	-0.14	-0.07			
O75995	SAM and SH3 domain-containing protein 3	10	67	-0.06	0.08	0.11			
Q9NSI8	SAM domain-containing protein SAMSN-1	5	13	-0.13	0.06	0.12			
P82979	SAP domain-containing ribonucleoprotein	11	84	-0.30	-0.14	0.19			
Q9UHR5	SAP30-binding protein	5	28	-0.21	-0.24	0.20			
P16615	Sarcoplasmic/endoplasmic reticulum calcium ATPase 2	12	61	-0.05	0.43	0.42			

Q93084	Sarcoplasmic/endoplasmic reticulum calcium ATPase 3	18	169	0.15	0.30	0.08			
Q9UL12	Sarcosine dehydrogenase, mitochondrial	1	1	0.47	0.81	0.35			
Q15424	Scaffold attachment factor B1	11	114	-0.18	-0.22	-0.10			
Q14151	Scaffold attachment factor B2	9	91	-0.03	-0.22	-0.41			
Q7Z7L1	Schlafen family member 11	1	20	0.18	0.21	0.04			
Q08AF3	Schlafen family member 5	17	181	-0.20	-0.04	0.00			
Q6P3W7	SCY1-like protein 2	1	3	0.02	0.01	0.00			
Q8WVM8	Sec1 family domain-containing protein 1	14	51	0.09	0.05	-0.01			
O76054	SEC14-like protein 2	2	2	0.10	-1.18	-1.29			
Q9Y6Y8	SEC23-interacting protein	5	10	-0.07	0.07	0.02			
Q12765	Secernin-1	9	53	0.94	1.07	0.10	5	5	
Q96FV2	Secernin-2	2	4	-0.39	-0.10	0.41			
P55000	Secreted Ly-6/uPAR-related protein 1	1	1	-0.34	-2.12	-1.80			
O15126	Secretory carrier-associated membrane protein 1	4	7	-0.17	0.19	0.37			
O15127	Secretory carrier-associated membrane protein 2	3	17	-0.47	0.12	0.51			
O14828	Secretory carrier-associated membrane protein 3	4	27	-0.18	-0.26	-0.05			
Q9UHJ6	Sedoheptulokinase	6	14	-0.10	-0.10	0.02			
O14641	Segment polarity protein dishevelled homolog DVL-2	1	7	0.02	0.02	0.01			
Q92997	Segment polarity protein dishevelled homolog DVL-3	1	7	0.20	0.38	0.18			
P49903	Selenide, water dikinase 1	8	41	0.10	-0.28	-0.39			
Q99611	Selenide, water dikinase 2	1	2	-0.12	-0.10	0.01			
Q93073	Selenocysteine insertion sequence-binding protein 2-like	1	1	0.31	0.12	-0.19			
Q96115	Selenocysteine lyase	9	56	0.02	-0.10	-0.27			
P57772	Selenocysteine-specific elongation factor	8	42	0.00	-0.15	-0.24			
Q8IZQ5	Selenoprotein H	8	54	0.11	-0.64	-0.62		5	4
Q9BVL4	Selenoprotein O	1	1	-0.08	0.02	0.10			
Q9BQE4	Selenoprotein S	2	3	0.01	0.32	0.26			
P63302	Selenoprotein W	1	1	-0.28	-0.28	-0.02			
Q92854	Semaphorin-4D	4	4	0.12	0.15	0.03			
Q9P0U3	Sentrin-specific protease 1	2	2	-0.11	0.18	0.29			
Q9H4L4	Sentrin-specific protease 3	4	8	-0.24	-0.15	0.02			
Q9BQF6	Sentrin-specific protease 7	4	12	-0.10	-0.21	0.04			
Q8WYJ6	Septin-1	17	154	-0.10	-0.20	-0.21			
Q9NVA2	Septin-11	6	119	-0.45	-0.32	0.37			
Q15019	Septin-2	18	226	-0.06	0.14	0.09			
O43236	Septin-4	1	1	NA	NA	NA			
Q14141	Septin-6	13	232	0.08	-0.13	-0.09			
Q16181	Septin-7	22	220	-0.06	-0.10	0.08			
Q9UHD8	Septin-9	31	294	-0.12	-0.14	-0.13			
Q13501	Sequestosome-1	4	16	-0.21	0.22	0.51			
P83111	Serine beta-lactamase-like protein LACTB, mitochondrial	7	17	0.15	0.28	-0.01			
P34896	Serine hydroxymethyltransferase, cytosolic	2	6	0.02	0.14	0.13			
P34897	Serine hydroxymethyltransferase, mitochondrial	15	61	-0.07	0.33	0.31			
O15269	Serine palmitoyltransferase 1	2	4	-0.31	-0.13	0.19			
O15270	Serine palmitoyltransferase 2	1	1	-0.55	0.31	0.86			
P83110	Serine protease HTRA3	1	2	-0.18	0.02	0.20			
Q8IYB3	Serine/arginine repetitive matrix protein 1	7	34	0.03	-0.29	-0.04			
Q9UQ35	Serine/arginine repetitive matrix protein 2	30	233	-0.25	-0.03	0.17			
Q961Z7	Serine/Arginine-related protein 53	2	3	-0.06	-0.50	0.03			
Q07955	Serine/arginine-rich splicing factor 1	15	265	-0.19	-0.18	-0.03			
O75494	Serine/arginine-rich splicing factor 10	5	25	-0.47	-0.19	0.29			
Q05519	Serine/arginine-rich splicing factor 11	6	72	-0.16	-0.15	-0.01			
Q01130	Serine/arginine-rich splicing factor 2	6	168	-0.04	-0.09	-0.06			
P84103	Serine/arginine-rich splicing factor 3	7	38	-0.05	-0.06	-0.24			
Q08170	Serine/arginine-rich splicing factor 4	5	55	-0.31	-0.13	0.17			
Q13243	Serine/arginine-rich splicing factor 5	5	43	-0.10	-0.21	-0.37			
Q13247	Serine/arginine-rich splicing factor 6	3	53	-0.03	-0.32	-0.03			
Q16629	Serine/arginine-rich splicing factor 7	7	70	-0.04	-0.11	0.05			
Q9BRL6	Serine/arginine-rich splicing factor 8	1	43	0.08	-0.43	-0.45			
Q13242	Serine/arginine-rich splicing factor 9	5	20	-0.50	-0.32	0.19			
O94804	Serine/threonine-protein kinase 10	26	201	-0.46	0.25	0.73			5
Q8N1F8	Serine/threonine-protein kinase 11-interacting protein	2	5	0.03	0.15	0.29			
O94768	Serine/threonine-protein kinase 17B	2	3	0.26	-0.25	-0.51			
Q9Y6E0	Serine/threonine-protein kinase 24	8	67	0.53	0.28	-0.17			
Q86UX6	Serine/threonine-protein kinase 32C	1	1	-0.33	-0.17	0.17			
Q15208	Serine/threonine-protein kinase 38	7	25	-0.19	0.02	0.19			
Q9Y2H1	Serine/threonine-protein kinase 38-like	1	4	NA	NA	NA			
Q13043	Serine/threonine-protein kinase 4	25	185	0.00	-0.03	0.01			
P10398	Serine/threonine-protein kinase A-Raf	4	22	-0.28	-0.03	0.09			
Q9BZL6	Serine/threonine-protein kinase D2	5	48	-0.44	-0.14	0.18			
Q8IWU2	Serine/threonine-protein kinase LMTK2	1	1	0.20	-0.29	-0.49			
Q7KZ17	Serine/threonine-protein kinase MARK2	8	25	-0.17	-0.01	0.15			
Q9P289	Serine/threonine-protein kinase mTOR	8	106	-0.16	0.01	0.16			
P42345	Serine/threonine-protein kinase mTOR	5	16	-0.13	-0.16	-0.09			
Q16512	Serine/threonine-protein kinase N1	18	88	-0.32	0.02	0.40			
Q96PY6	Serine/threonine-protein kinase Nek1	1	1	-0.01	-0.24	-0.22			
Q6ZWH5	Serine/threonine-protein kinase Nek10	1	13	-0.21	-0.32	-0.16			
P51957	Serine/threonine-protein kinase Nek4	1	1	NA	NA	NA			
Q8TDX7	Serine/threonine-protein kinase Nek7	7	34	0.59	0.54	-0.15	5	5	
Q8TD19	Serine/threonine-protein kinase Nek9	16	65	0.15	-0.20	-0.40			
O95747	Serine/threonine-protein kinase OSR1	9	51	0.20	0.16	-0.06			
Q13153	Serine/threonine-protein kinase PAK 1	4	44	-0.20	-0.70	-0.30		5	
Q13177	Serine/threonine-protein kinase PAK 2	20	220	0.12	0.08	-0.07			
Q13523	Serine/threonine-protein kinase PRP4 homolog	12	24	-0.18	-0.12	0.03			
Q9Y2K2	Serine/threonine-protein kinase SIK3	2	4	0.30	0.24	0.03			
Q96Q15	Serine/threonine-protein kinase SMG1	1	8	-0.13	0.21	0.34			

Q9UL54	Serine/threonine-protein kinase TAO2	1	2	-0.10	-0.06	0.04			
Q9H2K8	Serine/threonine-protein kinase TAO3	11	29	-0.32	0.03	0.39			
Q9UHD2	Serine/threonine-protein kinase TBK1	6	26	0.12	0.66	0.29		5	
Q9UKI8	Serine/threonine-protein kinase tousled-like 1	2	7	0.23	0.03	-0.20			
Q86UE8	Serine/threonine-protein kinase tousled-like 2	2	7	-1.98	-0.90	1.09			
O75385	Serine/threonine-protein kinase ULK1	1	1	-0.30	0.44	0.76			
Q6PHR2	Serine/threonine-protein kinase ULK3	1	1	NA	NA	NA			
Q99986	Serine/threonine-protein kinase VRK1	4	6	-0.07	-0.19	-0.25			
Q9H4A3	Serine/threonine-protein kinase WNK1	11	27	0.11	-0.09	-0.17			
O75460	Serine/threonine-protein kinase/endoribonuclease IRE1	1	1	0.90	1.65	0.73			
Q96QC0	Serine/threonine-protein phosphatase 1 regulatory subunit 10	2	4	-0.16	-0.11	0.05			
P63151	Serine/threonine-protein phosphatase 2A 55 kDa regulatory subunit B alpha isoform	12	29	-0.02	0.08	-0.03			
Q15172	Serine/threonine-protein phosphatase 2A 56 kDa regulatory subunit alpha isoform	3	7	-0.09	0.30	0.36			
Q14738	Serine/threonine-protein phosphatase 2A 56 kDa regulatory subunit delta isoform	2	9	0.12	-0.04	0.16			
Q16537	Serine/threonine-protein phosphatase 2A 56 kDa regulatory subunit epsilon isoform	2	7	-0.21	0.13	0.35			
Q13362	Serine/threonine-protein phosphatase 2A 56 kDa regulatory subunit gamma isoform	1	8	-0.02	0.04	0.07			
P30153	Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A alpha isoform	16	169	0.02	0.10	0.13			
P30154	Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A beta isoform	2	36	-0.11	-0.15	-0.05			
Q15257	Serine/threonine-protein phosphatase 2A activator	6	15	-0.18	0.14	0.24			
P67775	Serine/threonine-protein phosphatase 2A catalytic subunit alpha isoform	6	12	-0.23	-0.03	0.14			
Q08209	Serine/threonine-protein phosphatase 2B catalytic subunit alpha isoform	5	35	-0.06	0.57	0.60	5		4
P16298	Serine/threonine-protein phosphatase 2B catalytic subunit beta isoform	6	38	-0.17	-0.07	0.03			
P48454	Serine/threonine-protein phosphatase 2B catalytic subunit gamma isoform	4	15	-0.17	-0.33	-0.21			
P60510	Serine/threonine-protein phosphatase 4 catalytic subunit	1	3	-0.35	0.07	0.35			
Q8TF05	Serine/threonine-protein phosphatase 4 regulatory subunit 1	4	5	0.24	0.42	0.19			
Q9NY27	Serine/threonine-protein phosphatase 4 regulatory subunit 2	4	6	0.00	0.03	0.09			
Q6IN85	Serine/threonine-protein phosphatase 4 regulatory subunit 3A	7	31	-0.18	-0.11	0.02			
Q5MIZ7	Serine/threonine-protein phosphatase 4 regulatory subunit 3B	1	10	-0.67	-0.28	0.39			
P53041	Serine/threonine-protein phosphatase 5	14	64	-0.25	0.00	0.20			
O00743	Serine/threonine-protein phosphatase 6 catalytic subunit	4	15	-0.04	-0.09	-0.04			
O15084	Serine/threonine-protein phosphatase 6 regulatory ankyrin repeat subunit A	1	18	-0.07	0.04	0.11			
Q8N8A2	Serine/threonine-protein phosphatase 6 regulatory ankyrin repeat subunit B	22	104	0.08	0.07	-0.01			
Q9UPN7	Serine/threonine-protein phosphatase 6 regulatory subunit 1	7	29	-0.01	0.03	0.24			
O75170	Serine/threonine-protein phosphatase 6 regulatory subunit 2	8	21	-0.08	-0.04	0.22			
Q5H9R7	Serine/threonine-protein phosphatase 6 regulatory subunit 3	1	1	0.40	0.42	0.00			
Q96HS1	Serine/threonine-protein phosphatase PGAM5, mitochondrial	6	16	-0.14	0.09	0.16			
P62136	Serine/threonine-protein phosphatase PP1-alpha catalytic subunit	4	55	-0.27	0.18	0.42			
P62140	Serine/threonine-protein phosphatase PP1-beta catalytic subunit	1	51	0.20	0.23	0.03			
P36873	Serine/threonine-protein phosphatase PP1-gamma catalytic subunit	1	31	-0.22	0.06	0.28			
Q13315	Serine-protein kinase ATM	30	91	0.12	-0.19	-0.28			
Q9H7U1	Serine-rich coiled-coil domain-containing protein 2	1	1	0.03	0.46	0.43			
Q9Y3F4	Serine-threonine kinase receptor-associated protein	11	56	0.02	-0.01	-0.04			
P49591	Serine--tRNA ligase, cytoplasmic	9	40	0.15	-0.17	-0.23			
Q9NP81	Serine--tRNA ligase, mitochondrial	11	19	-0.01	-0.03	0.08			
Q96C92	Serologically defined colon cancer antigen 3	1	1	-0.09	-0.26	-0.16			
P48595	Serpin B10	1	4	0.14	-0.52	-0.68			
Q96P63	Serpin B12	1	2	0.69	0.51	-0.17			
P29508	Serpin B3	5	10	1.85	0.79	-0.91			
P35237	Serpin B6	13	105	-0.57	-0.48	0.17			
P50452	Serpin B8	5	81	0.18	-0.01	-0.29			
P50453	Serpin B9	24	270	0.49	0.09	-0.62	4		3
P50454	Serpin H1	1	6	-0.21	0.06	0.26			
Q9BXP5	Serrate RNA effector molecule homolog	19	102	0.00	-0.22	-0.22			
P02768	Serum albumin	14	406	0.63	0.21	-0.16	5		
O95810	Serum deprivation-response protein	6	17	-0.46	-0.49	0.09			
Q15165	Serum paraoxonase/arylesterase 2	1	1	-0.73	0.20	0.93			
P11831	Serum response factor	2	10	-0.09	-0.02	-0.07			
Q8NEF9	Serum response factor-binding protein 1	2	4	0.23	-0.13	-0.31			
Q6GMV2	SET and MYND domain-containing protein 5	1	1	0.60	-0.47	-1.07			
Q9UBL3	Set1/Ash2 histone methyltransferase complex subunit ASH2	2	9	0.01	-0.11	-0.16			
Q8N228	Sex comb on midleg-like protein 4	1	5	NA	NA	NA			
P10768	S-formylglutathione hydrolase	8	63	0.42	-0.17	-0.67			5
O60880	SH2 domain-containing protein 1A	4	8	-0.24	0.43	0.37			
Q9NP31	SH2 domain-containing protein 2A	6	17	-0.11	0.80	1.29	4		5
Q8N5H7	SH2 domain-containing protein 3C	2	8	-0.66	0.41	0.99	4	5	5
O75368	SH3 domain-binding glutamic acid-rich-like protein	11	105	-0.10	-0.26	0.01			
Q9H299	SH3 domain-binding glutamic acid-rich-like protein 3	5	146	-0.72	-0.31	0.45	3		
Q9Y3L3	SH3 domain-binding protein 1	21	225	-0.16	-0.15	0.05			
Q7L8J4	SH3 domain-binding protein 5-like	1	1	NA	NA	NA			
Q96B97	SH3 domain-containing kinase-binding protein 1	30	216	0.00	-0.14	-0.08			
Q8TBC3	SH3KBP1-binding protein 1	1	2	-0.11	0.27	0.36			
Q9H0F6	Sharpin	4	7	0.20	0.11	0.06			
P29353	SHC-transforming protein 1	3	7	0.16	0.33	0.15			
P45954	Short/branched chain specific acyl-CoA dehydrogenase, mitochondrial	7	17	0.07	0.06	-0.05			
Q8NEX9	Short-chain dehydrogenase/reductase family 9C member 7	2	2	2.48	1.68	-0.80			
P16219	Short-chain specific acyl-CoA dehydrogenase, mitochondrial	11	84	-0.26	-0.12	0.03			
Q9NR45	Sialic acid synthase	8	29	0.30	0.22	-0.11			
Q9Y286	Sialic acid-binding Ig-like lectin 7	3	5	-0.57	0.70	1.04			3
Q9Y336	Sialic acid-binding Ig-like lectin 9	2	4	-0.49	0.31	0.68			
Q9H9B4	Sideroflexin-1	12	86	0.42	-0.58	-0.93		4	5
Q9BWM7	Sideroflexin-3	6	40	0.11	0.50	0.45		5	
Q15005	Signal peptidase complex subunit 2	5	27	0.15	0.50	0.27			
P61009	Signal peptidase complex subunit 3	3	14	0.20	0.60	0.44		3	
P37108	Signal recognition particle 14 kDa protein	12	129	-0.04	-0.50	-0.54		5	5
P09132	Signal recognition particle 19 kDa protein	3	12	0.07	-0.03	-0.28			
P61011	Signal recognition particle 54 kDa protein	10	40	0.28	0.06	-0.23			

P49458	Signal recognition particle 9 kDa protein	7	30	0.17	-0.21	-0.44			
P08240	Signal recognition particle receptor subunit alpha	13	32	0.66	0.43	-0.22	3	5	
Q9Y5M8	Signal recognition particle receptor subunit beta	4	23	0.60	0.34	-0.13	4		
Q9UHB9	Signal recognition particle subunit SRP68	14	35	0.18	0.08	-0.21			
O76094	Signal recognition particle subunit SRP72	16	40	0.36	0.12	-0.06			
P42224	Signal transducer and activator of transcription 1-alpha/beta	28	148	0.20	-0.31	-0.50			4
P52630	Signal transducer and activator of transcription 2	4	16	-0.07	0.13	0.27			
P40763	Signal transducer and activator of transcription 3	10	24	0.10	0.10	0.01			
Q14765	Signal transducer and activator of transcription 4	7	23	0.04	0.72	0.40		5	
P42229	Signal transducer and activator of transcription 5A	4	44	0.37	-0.13	-0.56			
P51692	Signal transducer and activator of transcription 5B	3	46	0.83	0.39	-0.35	5		
P42226	Signal transducer and activator of transcription 6	3	12	-0.03	-0.15	-0.15			
Q92783	Signal transducing adapter molecule 1	3	5	-0.24	0.11	0.24			
O75886	Signal transducing adapter molecule 2	2	2	-0.30	0.37	0.66			
O43166	Signal-induced proliferation-associated 1-like protein 1	7	8	0.26	0.54	0.13		3	
Q96FS4	Signal-induced proliferation-associated protein 1	27	130	-0.03	0.30	0.34			
Q13291	Signaling lymphocytic activation molecule	1	1	2.15	1.73	-0.43			
Q9Y3P8	Signaling threshold-regulating transmembrane adapter 1	6	22	1.01	0.17	-0.90	4		4
Q5TFQ8	Signal-regulatory protein beta-1 isoform 3	1	1	0.55	0.83	0.29			
Q9P1W8	Signal-regulatory protein gamma	2	2	-0.14	-0.13	0.01			
Q9H7L9	Sin3 histone deacetylase corepressor complex component SDS3	3	3	-0.62	-0.53	0.15			
Q6IA17	Single Ig IL-1-related receptor	4	19	-0.47	0.48	0.99		4	5
Q9BWW4	Single-stranded DNA-binding protein 3	2	3	-0.73	-0.03	0.70			
Q9BWG4	Single-stranded DNA-binding protein 4	2	2	-0.23	1.28	1.49			
Q04837	Single-stranded DNA-binding protein, mitochondrial	10	74	0.39	-0.15	-0.37			
Q29RF7	Sister chromatid cohesion protein PDS5 homolog A	24	103	-0.03	-0.12	-0.10			
Q9NTI5	Sister chromatid cohesion protein PDS5 homolog B	23	70	-0.11	-0.08	0.01			
O43805	Sjogren syndrome nuclear autoantigen 1	1	1	0.05	0.51	0.47			
Q9P270	SLAIN motif-containing protein 2	13	35	-0.14	0.10	0.27			
Q9UIB8	SLAM family member 5	1	1	0.36	-0.31	-0.67			
Q96DU3	SLAM family member 6	4	15	0.08	0.46	0.41			
Q9NR83	SLC2A4 regulator	1	2	NA	NA	NA			
Q9H5Y7	SLIT and NTRK-like protein 6	1	2	-0.10	-0.15	-0.05			
Q8TAD8	Smad nuclear-interacting protein 1	3	5	-0.07	-0.15	0.01			
O00193	Small acidic protein	3	9	-0.43	-0.06	0.44			
P84101	Small EDRK-rich factor 2	2	5	0.28	0.14	-0.14			
O43765	Small glutamine-rich tetratricopeptide repeat-containing protein alpha	5	30	0.14	-0.03	-0.12			
Q96EQ0	Small glutamine-rich tetratricopeptide repeat-containing protein beta	2	3	0.30	-0.78	-1.07			
Q96EX1	Small integral membrane protein 12	1	1	-0.02	-0.14	-0.12			
Q8N5G0	Small integral membrane protein 20	1	9	0.00	-0.02	-0.12			
P62304	Small nuclear ribonucleoprotein E	4	34	-0.16	-0.14	-0.07			
P62306	Small nuclear ribonucleoprotein F	3	193	-0.30	-0.43	-0.22		4	
A8MWD9	Small nuclear ribonucleoprotein G-like protein	4	42	-0.38	-0.41	-0.20		5	
P62314	Small nuclear ribonucleoprotein Sm D1	2	30	-0.06	0.02	-0.11			
P62316	Small nuclear ribonucleoprotein Sm D2	7	117	-0.15	-0.20	-0.12			
P62318	Small nuclear ribonucleoprotein Sm D3	8	118	-0.19	-0.13	0.00			
P14678	Small nuclear ribonucleoprotein-associated proteins B and B'	5	165	-0.30	-0.23	0.05			
O75691	Small subunit processome component 20 homolog	5	12	0.33	-0.14	-0.40			
P63165	Small ubiquitin-related modifier 1	2	9	-0.22	-0.16	-0.12			
P61956	Small ubiquitin-related modifier 2	1	50	-0.41	0.07	0.47			
P55854	Small ubiquitin-related modifier 3	1	50	-1.09	-0.60	0.50			
Q8NHG7	Small VCP/p97-interacting protein	1	8	0.51	-0.12	-0.69			
Q13126	S-methyl-5'-thioadenosine phosphorylase	8	44	0.64	-0.09	-0.68	3		5
O95295	SNARE-associated protein Snapin	5	23	-0.12	0.13	0.26			
Q9NRH2	SNF-related serine/threonine-protein kinase	1	1	1.06	-0.21	-1.27			
Q13573	SNW domain-containing protein 1	14	53	-0.20	-0.20	0.11			
Q9Y6M7	Sodium bicarbonate cotransporter 3	1	2	0.38	-0.10	-0.48			
Q8NBS3	Sodium bicarbonate transporter-like protein 11	1	2	-0.08	-0.49	-0.40			
P05023	Sodium/potassium-transporting ATPase subunit alpha-1	26	165	0.62	0.37	-0.20			
P54709	Sodium/potassium-transporting ATPase subunit beta-3	3	8	0.68	0.18	-0.48	3		
Q9Y6X4	Soluble lamin-associated protein of 75 kDa	8	27	0.01	0.06	0.11			
Q9UHW9	Solute carrier family 12 member 6	1	3	NA	NA	NA			
P11166	Solute carrier family 2, facilitated glucose transporter member 1	1	6	-0.20	0.23	0.54			
P11169	Solute carrier family 2, facilitated glucose transporter member 3	2	15	0.04	0.55	0.52			
Q96AG3	Solute carrier family 25 member 46	3	10	-0.19	-0.07	0.14			
Q8N357	Solute carrier family 35 member F6	1	4	-0.20	0.34	0.54			
Q9UIG8	Solute carrier organic anion transporter family member 3A1	1	1	0.25	0.86	0.61			
Q9NQZ2	Something about silencing protein 10	4	8	0.46	-0.17	-0.81			
Q00796	Sorbitol dehydrogenase	4	14	0.06	-0.11	-0.16			
P30626	Sorcin	5	39	0.36	0.15	0.06			
Q92673	Sortilin-related receptor	5	9	-0.02	0.32	0.30			
Q9Y512	Sorting and assembly machinery component 50 homolog	4	8	-0.28	-0.46	-0.18			
Q13596	Sorting nexin-1	8	48	-0.35	0.19	0.50			
Q9Y5W9	Sorting nexin-11	2	3	0.27	0.31	0.05			
Q9UMY4	Sorting nexin-12	3	25	-0.43	0.00	0.32			
Q9NRS6	Sorting nexin-15	2	3	0.13	0.07	-0.06			
Q15036	Sorting nexin-17	2	12	-0.22	0.09	0.42			
Q96RF0	Sorting nexin-18	6	20	-1.53	-0.38	1.40	5		5
O60749	Sorting nexin-2	12	64	0.08	0.00	-0.06			
Q96L92	Sorting nexin-27	2	6	-0.05	0.17	0.24			
O60493	Sorting nexin-3	5	30	-0.51	0.03	0.61	5		5
O95219	Sorting nexin-4	1	1	0.04	-0.05	-0.10			
Q9Y5X3	Sorting nexin-5	8	19	0.15	0.41	0.22			
Q9UNH7	Sorting nexin-6	14	68	-0.15	0.09	0.19			
Q9Y5X1	Sorting nexin-9	2	7	0.96	-0.18	-1.02	3		4
Q9NRY2	SOSS complex subunit C	1	4	-0.46	-0.13	0.42			

Q9HB58	Sp110 nuclear body protein	11	18	-0.11	-0.28	-0.06			
Q8N0X7	Spartin	1	3	0.13	-0.44	-0.61			
Q9UBP0	Spastin	2	8	0.08	0.01	-0.08			
Q96J17	Spatacsin	1	4	0.16	0.12	-0.15			
Q9NUQ6	SPATS2-like protein	1	1	0.60	1.22	0.62			
Q13813	Spectrin alpha chain, non-erythrocytic 1	107	454	0.27	-0.42	-0.59		4	5
P11277	Spectrin beta chain, erythrocytic	1	3	-1.52	-1.56	-0.03			
Q01082	Spectrin beta chain, non-erythrocytic 1	90	624	0.21	-0.49	-0.73		5	5
O75391	Sperm-associated antigen 7	6	11	-0.09	-0.14	-0.07			
Q96N96	Spermatogenesis-associated protein 13	2	9	-0.55	0.27	0.78			4
Q8TB22	Spermatogenesis-associated protein 20	2	2	0.03	0.10	0.07			
Q8NB90	Spermatogenesis-associated protein 5	4	30	0.33	0.15	-0.29			
Q9BVQ7	Spermatogenesis-associated protein 5-like protein 1	4	9	0.03	-0.06	-0.18			
Q9H9C1	Spermatogenesis-defective protein 39 homolog	1	3	0.01	0.14	0.06			
P19623	Spermidine synthase	9	27	0.84	-0.17	-0.75		5	4
P52788	Spermine synthase	2	3	-0.20	-0.24	-0.03			
P63208	S-phase kinase-associated protein 1	6	28	-0.01	0.16	0.06			
Q9H228	Sphingosine 1-phosphate receptor 5	1	1	0.46	1.39	0.94			
O95470	Sphingosine-1-phosphate lyase 1	8	18	0.05	0.29	0.26			
Q9BX95	Sphingosine-1-phosphate phosphatase 1	2	6	-0.41	-0.01	0.40			
Q8N0Z3	Spindle and centriole-associated protein 1	1	1	0.49	0.15	-0.33			
Q9Y657	Spindlin-1	4	9	-0.22	-0.32	-0.10			
Q13838	Spliceosome RNA helicase DDX39B	6	139	0.00	-0.08	-0.09			
Q9P013	Spliceosome-associated protein CWC15 homolog	4	27	-0.25	-0.22	0.09			
Q15637	Splicing factor 1	13	120	-0.16	-0.03	0.00			
Q15459	Splicing factor 3A subunit 1	28	122	-0.15	-0.16	-0.02			
Q15428	Splicing factor 3A subunit 2	8	31	-0.17	-0.29	0.04			
Q12874	Splicing factor 3A subunit 3	12	79	-0.06	-0.12	-0.16			
O75533	Splicing factor 3B subunit 1	37	165	-0.01	-0.12	-0.02			
Q13435	Splicing factor 3B subunit 2	35	236	0.01	-0.14	0.00			
Q15393	Splicing factor 3B subunit 3	28	156	0.02	-0.03	-0.02			
Q15427	Splicing factor 3B subunit 4	3	9	0.02	0.02	-0.01			
Q9BWJ5	Splicing factor 3B subunit 5	2	3	-1.49	-0.75	0.75			
Q96I25	Splicing factor 45	13	45	-0.32	-0.17	0.10			
Q01081	Splicing factor U2AF 35 kDa subunit	3	22	-0.12	0.27	0.29			
P26368	Splicing factor U2AF 65 kDa subunit	11	67	-0.09	-0.04	0.05			
O95104	Splicing factor, arginine/serine-rich 15	6	21	-0.09	-0.24	0.06			
Q9H7N4	Splicing factor, arginine/serine-rich 19	9	29	-0.02	-0.03	0.18			
P23246	Splicing factor, proline- and glutamine-rich	35	428	-0.10	-0.06	-0.07			
Q12872	Splicing factor, suppressor of white-apricot homolog	4	5	-0.16	-0.10	-0.03			
Q8WXA9	Splicing regulatory glutamine/lysine-rich protein 1	5	9	-0.35	-0.26	-0.02			
Q8WW59	SPRY domain-containing protein 4	1	2	0.61	0.23	-0.37			
Q5W111	SPRY domain-containing protein 7	1	1	-0.05	0.33	0.36			
Q15020	Squamous cell carcinoma antigen recognized by T-cells 3	22	107	0.01	-0.22	-0.10			
Q9GZT3	SRA stem-loop-interacting RNA-binding protein, mitochondrial	3	10	0.19	0.08	-0.20			
Q86WV1	Src kinase-associated phosphoprotein 1	5	34	-0.22	-1.31	-1.19		5	5
O75563	Src kinase-associated phosphoprotein 2	3	5	-0.19	0.23	0.42			
Q14247	Src substrate cortactin	1	3	0.00	-0.01	0.11			
Q9H6Q3	Src-like-adaptor 2	1	2	-0.73	0.15	0.86			
Q96SB4	SRSF protein kinase 1	3	8	0.26	0.41	0.15			
P78362	SRSF protein kinase 2	4	11	-0.53	-0.11	0.40			
Q9UHA2	SS18-like protein 2	1	1	0.21	0.20	-0.01			
O95630	STAM-binding protein	4	9	0.38	0.27	-0.09			
Q7KZF4	Staphylococcal nuclease domain-containing protein 1	34	239	0.60	0.38	-0.12		5	
Q9NSY2	STAR-related lipid transfer protein 5	1	1	0.56	-0.19	-0.74			
P16949	Stathmin	11	66	-1.08	-0.67	0.33		5	5
Q9UEW8	STE20/SPS1-related proline-alanine-rich protein kinase	3	8	-0.16	0.06	0.41			
Q9H2G2	STE20-like serine/threonine-protein kinase	20	87	-0.08	0.28	0.36			5
Q6SZW1	Sterile alpha and TIR motif-containing protein 1	2	7	0.00	-0.15	-0.24			
Q5K651	Sterile alpha motif domain-containing protein 9	7	26	-0.16	0.27	0.24			
Q9HD15	Steroid receptor RNA activator 1	4	11	-0.31	-0.17	0.18			
Q15738	Sterol-4-alpha-carboxylate 3-dehydrogenase, decarboxylating	3	3	-0.17	0.07	0.23			
Q86WV6	Stimulator of interferon genes protein	2	6	-0.33	-0.20	0.15			
Q9UJZ1	Stomatin-like protein 2, mitochondrial	11	49	0.05	0.16	0.06			
Q96BY9	Store-operated calcium entry-associated regulatory factor	1	1	0.05	-0.19	-0.24			
P38646	Stress-70 protein, mitochondrial	41	399	0.03	-0.16	-0.16			
P31948	Stress-induced-phosphoprotein 1	36	215	0.09	-0.12	-0.14			
O43815	Striatin	15	84	-0.42	0.05	0.35			
Q13033	Striatin-3	2	10	-0.02	0.00	-0.05			
Q9NRL3	Striatin-4	4	14	-0.09	-0.10	0.13			
Q5VSL9	Striatin-interacting protein 1	5	26	-0.26	-0.09	0.16			
Q99470	Stromal cell-derived factor 2	1	1	NA	NA	NA			
Q9HCN8	Stromal cell-derived factor 2-like protein 1	2	6	-0.46	0.05	0.58			
Q13586	Stromal interaction molecule 1	19	51	-0.40	-0.10	0.31			
Q8IYB5	Stromal membrane-associated protein 1	1	4	0.12	0.72	0.59		3	
Q8WU79	Stromal membrane-associated protein 2	8	29	-0.19	-0.45	-0.20			
A6NHR9	Structural maintenance of chromosomes flexible hinge domain-containing p	35	114	0.01	-0.18	-0.18			
Q14683	Structural maintenance of chromosomes protein 1A	55	252	-0.12	-0.14	0.00			
O95347	Structural maintenance of chromosomes protein 2	2	2	-0.23	-0.04	0.19			
Q9UQE7	Structural maintenance of chromosomes protein 3	49	237	-0.14	-0.15	-0.06			
Q9NTJ3	Structural maintenance of chromosomes protein 4	1	1	-0.34	0.09	0.44			
Q8IY18	Structural maintenance of chromosomes protein 5	3	3	-0.25	0.04	0.27			
Q96SB8	Structural maintenance of chromosomes protein 6	1	3	-0.18	-0.38	-0.23			
Q9NX18	Succinate dehydrogenase assembly factor 2, mitochondrial	1	1	-0.73	-0.05	0.69			
P31040	Succinate dehydrogenase flavoprotein subunit, mitochondrial	19	122	0.34	0.08	-0.18			
P21912	Succinate dehydrogenase iron-sulfur subunit, mitochondrial	10	43	0.21	-0.18	-0.43			

P51649	Succinate-semialdehyde dehydrogenase, mitochondrial	9	43	0.29	-0.51	-0.80		4	5
P53597	Succinyl-CoA ligase subunit alpha, mitochondrial	12	107	0.12	-0.13	-0.19			
Q96199	Succinyl-CoA ligase subunit beta, mitochondrial	28	213	0.28	-0.18	-0.36			
Q9P2R7	Succinyl-CoA ligase subunit beta, mitochondrial	15	72	0.24	0.07	-0.13			
P55809	Succinyl-CoA:3-ketoacid coenzyme A transferase 1, mitochondrial	17	107	0.37	0.07	-0.37			
Q8NBK3	Sulfatase-modifying factor 1	1	1	-0.28	-0.11	0.15			
Q8NB7	Sulfatase-modifying factor 2	4	15	-0.51	-0.65	-0.18		3	
Q9Y6N5	Sulfide:quinone oxidoreductase, mitochondrial	26	179	0.39	0.61	0.03		4	
O43704	Sulfotransferase family cytosolic 1B member 1	4	8	-0.91	-1.14	-0.25	4	4	
Q9UBE0	SUMO-activating enzyme subunit 1	15	118	-0.12	-0.43	-0.29		4	
Q9UBT2	SUMO-activating enzyme subunit 2	16	66	-0.13	-0.36	-0.15			
P63279	SUMO-conjugating enzyme UBC9	5	17	-0.13	-0.28	0.06			
O94901	SUN domain-containing protein 1	1	12	-0.07	0.07	0.17			
Q9UH99	SUN domain-containing protein 2	25	127	-0.09	-0.04	0.18			
P42285	Superkiller viralicidic activity 2-like 2	11	36	0.13	-0.09	-0.24			
P00441	Superoxide dismutase	13	62	0.41	-0.04	-0.40			
P04179	Superoxide dismutase, mitochondrial	7	25	0.75	0.04	-0.83	4		4
O95425	Supervillin	7	17	0.06	0.10	-0.17			
Q9Y2Z0	Suppressor of G2 allele of SKP1 homolog	11	27	-0.06	-0.02	0.09			
Q9BRV8	Suppressor of IKBKE 1	2	4	-0.48	0.40	0.88			3
Q9NQ55	Suppressor of SWI4 1 homolog	5	6	-0.03	-0.78	-0.75			
Q8TDW4	Suppressor of tumorigenicity 7 protein-like	1	1	0.12	-0.21	-0.33			
Q6UWP8	Suprabasin	2	10	0.03	-0.10	-0.03			
Q15526	Surfeit locus protein 1	1	1	0.14	-0.01	-0.15			
Q15527	Surfeit locus protein 2	1	4	0.38	-0.32	-0.59			
O75683	Surfeit locus protein 6	8	14	0.53	-0.01	-0.43			
Q8IWZ8	SURP and G-patch domain-containing protein 1	7	19	-0.09	-0.19	-0.03			
Q8IX01	SURP and G-patch domain-containing protein 2	5	6	-0.36	-0.05	0.36			
Q16637	Survival motor neuron protein	1	1	0.38	-0.45	-0.83			
O75940	Survival of motor neuron-related-splicing factor 30	5	30	-0.12	-0.13	0.15			
Q7Z422	SUZ domain-containing protein 1	3	7	-0.40	-0.09	0.44			
Q92922	SWI/SNF complex subunit SMARCC1	2	49	-0.06	0.15	0.21			
Q8TAQ2	SWI/SNF complex subunit SMARCC2	20	138	-0.15	-0.04	0.07			
O60264	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin	21	76	0.12	-0.15	-0.20			
Q9NZC9	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin	2	5	-0.19	-0.08	0.08			
Q12824	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin	5	17	0.13	0.06	-0.06			
Q96GM5	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin	3	11	-0.02	0.17	-0.34			
Q92925	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin	9	18	-0.12	0.09	0.15			
Q969G3	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin	11	49	-0.39	-0.03	0.29			
Q9P0W2	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin	1	1	-0.47	0.07	0.55			
Q9UH65	Switch-associated protein 70	1	3	-0.59	-0.31	0.28			
Q92797	Symplekin	9	18	-0.02	-0.06	-0.05			
Q96A49	Synapse-associated protein 1	2	2	0.11	0.17	0.06			
Q99536	Synaptic vesicle membrane protein VAT-1 homolog	8	38	-0.17	0.45	0.55		4	4
O15498	Synaptobrevin homolog YKT6	4	14	0.15	0.37	0.24			
O43426	Synaptotagmin-1	1	1	-0.17	-0.14	0.01			
O15056	Synaptotagmin-2	4	10	-0.13	0.20	0.34			
P57105	Synaptotagmin-2-binding protein	1	2	0.16	0.06	-0.09			
O00161	Synaptosomal-associated protein 23	4	18	-0.17	0.10	0.20			
O95721	Synaptosomal-associated protein 29	8	42	-0.42	0.35	0.73			5
Q8IYJ3	Synaptotagmin-like protein 1	8	43	-0.33	0.36	0.72		5	4
Q9HCH5	Synaptotagmin-like protein 2	13	36	0.07	0.96	0.82		5	5
Q4VX76	Synaptotagmin-like protein 3	2	4	-0.25	1.19	1.45			3
Q96C24	Synaptotagmin-like protein 4	1	2	-0.18	-0.27	-0.10			
Q9NPQ8	Synembryn-A	7	23	0.04	0.17	0.12			
O15061	Synemin	3	4	1.08	0.80	-0.20			
Q9UMZ2	Synergina gamma	10	11	0.02	0.00	-0.10			
O60499	Syntaxin-10	1	1	-0.18	-0.62	-0.43			
O75558	Syntaxin-11	2	3	-0.63	0.28	0.57			
Q86Y82	Syntaxin-12	1	2	-0.31	0.09	0.40			
O14662	Syntaxin-16	1	1	-0.46	0.01	0.48			
P56962	Syntaxin-17	1	1	0.66	0.10	-0.54			
Q12846	Syntaxin-4	6	18	0.16	0.22	0.08			
Q13190	Syntaxin-5	6	16	-0.16	0.17	0.30			
O43752	Syntaxin-6	1	1	-0.68	-0.29	0.40			
O15400	Syntaxin-7	7	29	-1.15	0.22	1.34	5		5
Q9UNK0	Syntaxin-8	4	6	0.15	0.18	0.16			
P61764	Syntaxin-binding protein 1	1	1	NA	NA	NA			
Q15833	Syntaxin-binding protein 2	15	39	-0.15	0.25	0.37			
O00186	Syntaxin-binding protein 3	13	37	0.46	0.37	-0.01			
Q5T5C0	Syntaxin-binding protein 5	4	12	-0.37	0.01	0.36			
O00560	Syntenin-1	1	3	NA	NA	NA			
Q9Y6J9	TAF6-like RNA polymerase II p300/CBP-associated factor-associated factor	1	4	0.24	0.11	-0.13			
Q9Y490	Talin-1	131	1787	-0.26	0.26	0.41			
Q9Y4G6	Talin-2	1	228	0.11	0.41	0.30			
Q8N9U0	Tandem C2 domains nuclear protein	1	1	0.11	0.14	0.03			
O15533	Tapasin	4	56	-0.20	0.26	0.30			
Q9BX59	Tapasin-related protein	1	2	-0.31	0.23	0.54			
Q4KMQ1	Taperin	1	1	-0.82	0.14	0.96			
Q13148	TAR DNA-binding protein 43	7	82	-0.09	-0.20	-0.10			
Q96GM8	Target of EGR1 protein 1	1	4	-0.06	-0.11	-0.06			
O60784	Target of Myb protein 1	3	12	-0.02	0.05	0.11			
Q9BPZ7	Target of rapamycin complex 2 subunit MAPKAP1	1	5	0.08	0.21	0.13			
Q9BVC4	Target of rapamycin complex subunit LST8	1	6	-0.20	-0.20	0.00			
P13686	Tartrate-resistant acid phosphatase type 5	1	1	-0.44	-0.02	0.42			
P82094	TATA element modulatory factor	6	11	0.09	0.29	0.28			

O14981	TATA-binding protein-associated factor 172	6	13	0.01	-0.10	-0.07			
Q92804	TATA-binding protein-associated factor 2N	5	23	0.04	0.29	0.25			
P20226	TATA-box-binding protein	2	4	-0.07	-0.16	-0.09			
Q86VP1	Tax1-binding protein 1	1	1	-0.03	-0.34	-0.29			
O14907	Tax1-binding protein 3	1	1	-0.92	-0.37	0.56			
Q8TEA7	TBC domain-containing protein kinase-like protein	1	1	-0.25	0.11	0.37			
Q86TI0	TBC1 domain family member 1	5	12	0.00	-0.17	-0.16			
Q9BXI6	TBC1 domain family member 10A	4	11	-0.08	-0.13	0.09			
Q4KMP7	TBC1 domain family member 10B	7	17	-0.27	0.17	0.34			
Q9NVG8	TBC1 domain family member 13	3	4	0.00	0.03	0.04			
Q8TC07	TBC1 domain family member 15	6	18	0.20	-0.06	-0.35			
Q9HA65	TBC1 domain family member 17	3	9	0.05	-0.16	-0.16			
Q8WUA7	TBC1 domain family member 22A	3	5	-0.02	0.01	0.27			
Q9NUY8	TBC1 domain family member 23	1	1	NA	NA	NA			
Q9ULP9	TBC1 domain family member 24	1	1	0.15	0.15	0.00			
Q9UPU7	TBC1 domain family member 2B	8	17	0.27	0.21	-0.17			
Q96DN5	TBC1 domain family member 31	1	3	0.37	0.00	-0.33			
O60343	TBC1 domain family member 4	1	5	0.31	-0.10	-0.41			
Q92609	TBC1 domain family member 5	14	40	-0.13	0.20	0.31			
Q66K14	TBC1 domain family member 9B	4	7	-0.11	0.11	0.27			
Q9UL17	T-box transcription factor TBX21	10	39	-1.29	0.35	1.31	5		5
Q8N103	T-cell activation Rho GTPase-activating protein	2	3	0.02	0.62	0.37			
P09564	T-cell antigen CD7	3	7	-0.55	0.11	0.79			4
P30203	T-cell differentiation antigen CD6	5	22	1.39	0.25	-1.04	4		5
P01848	T-cell receptor alpha chain C region	2	8	0.19	-0.88	-1.06			
P01850	T-cell receptor beta-1 chain C region	1	1	NA	NA	NA			
Q6PIZ9	T-cell receptor-associated transmembrane adapter 1	1	8	0.96	0.35	-0.58	4		
P06729	T-cell surface antigen CD2	6	19	0.51	0.13	0.08			
P04234	T-cell surface glycoprotein CD3 delta chain	1	12	1.22	1.01	-0.12			
P07766	T-cell surface glycoprotein CD3 epsilon chain	4	18	1.70	-0.07	-1.76	4		4
P20963	T-cell surface glycoprotein CD3 zeta chain	8	57	-0.63	0.24	0.96	4		5
P06127	T-cell surface glycoprotein CD5	9	27	0.78	-0.51	-1.28	4	4	5
P01732	T-cell surface glycoprotein CD8 alpha chain	4	27	1.28	-0.24	-1.59	4		4
P10966	T-cell surface glycoprotein CD8 beta chain	3	3	0.29	-0.59	-0.89			
P0C126	TCF3 fusion partner	1	1	0.07	0.05	-0.02			
P17987	T-complex protein 1 subunit alpha	28	294	0.21	-0.10	-0.32			
P78371	T-complex protein 1 subunit beta	34	421	0.17	-0.14	-0.34			
P50991	T-complex protein 1 subunit delta	32	248	0.23	-0.23	-0.44			
P48643	T-complex protein 1 subunit epsilon	27	206	0.18	-0.14	-0.29			
Q99832	T-complex protein 1 subunit eta	30	260	0.14	-0.18	-0.31			
P49368	T-complex protein 1 subunit gamma	31	313	0.20	-0.06	-0.34			
P50990	T-complex protein 1 subunit theta	38	434	0.19	-0.11	-0.25			
P40227	T-complex protein 1 subunit zeta	24	264	0.23	-0.17	-0.33			
Q9NUJ3	T-complex protein 11-like protein 1	1	1	0.45	0.74	0.29			
Q7Z6L1	Tectonin beta-propeller repeat-containing protein 1	3	9	-0.09	-0.62	-0.79	4		4
Q99973	Telomerase protein component 1	2	11	-0.21	-0.33	-0.11			
Q86US8	Telomerase-binding protein EST1A	1	1	-0.28	-0.06	0.22			
Q5UIP0	Telomere-associated protein RIF1	4	9	-0.13	-0.15	-0.13			
P54274	Telomeric repeat-binding factor 1	2	3	-0.34	0.07	0.41			
Q15554	Telomeric repeat-binding factor 2	9	34	-0.02	-0.10	-0.05			
Q9NYB0	Telomeric repeat-binding factor 2-interacting protein 1	10	57	-0.10	0.02	0.11			
Q5TAX3	Terminal uridylyltransferase 4	2	3	0.04	0.11	0.08			
Q5VY58	Terminal uridylyltransferase 7	1	6	-0.10	0.43	0.41			
Q92563	Testican-2	5	10	0.87	1.22	0.26	4		4
P0DJG4	Testicular haploid expressed gene protein-like	1	2	-1.15	-0.29	0.86			
Q9UGI8	Testin	28	240	-0.32	0.05	0.38			
Q9NXF1	Testis-expressed sequence 10 protein	3	69	0.01	-0.19	-0.19			
Q9Y6I9	Testis-expressed sequence 264 protein	1	11	-0.77	-0.20	0.25	3		
Q6SA08	Testis-specific serine/threonine-protein kinase 4	1	3	0.39	0.70	0.31			
Q9H0U9	Testis-specific Y-encoded-like protein 1	3	6	0.32	0.17	-0.10			
Q9BZE9	Tether containing UBX domain for GLUT4	3	4	-0.07	0.04	0.23			
P05452	Tetranectin	1	2	0.29	0.31	0.03			
Q8NG11	Tetraspanin-14	2	4	0.68	0.70	-0.15			
Q99614	Tetratricopeptide repeat protein 1	3	14	-0.06	-0.04	-0.11			
Q96N46	Tetratricopeptide repeat protein 14	1	1	-0.45	-0.46	0.00			
Q6P3X3	Tetratricopeptide repeat protein 27	1	1	-0.25	-0.01	0.24			
Q6PGP7	Tetratricopeptide repeat protein 37	7	15	0.36	0.05	-0.29			
Q5R3I4	Tetratricopeptide repeat protein 38	5	15	-0.74	0.56	1.17	3		4
Q8N584	Tetratricopeptide repeat protein 39C	2	4	-0.03	0.23	0.27			
Q95801	Tetratricopeptide repeat protein 4	2	6	0.07	-0.11	-0.15			
Q8IYW2	Tetratricopeptide repeat protein 40	1	25	NA	NA	NA			
Q92623	Tetratricopeptide repeat protein 9A	3	7	0.64	-0.05	-0.43			
Q8N5M4	Tetratricopeptide repeat protein 9C	1	1	-0.26	0.07	0.33			
P19447	TFIIH basal transcription factor complex helicase XPB subunit	3	5	0.06	-0.03	-0.10			
P18074	TFIIH basal transcription factor complex helicase XPD subunit	2	2	-0.28	-0.20	0.07			
P37173	TGF-beta receptor type-2	1	1	-0.03	-0.41	-0.37			
Q15750	TGF-beta-activated kinase 1 and MAP3K7-binding protein 1	7	16	0.00	-0.05	0.03			
Q9NYJ8	TGF-beta-activated kinase 1 and MAP3K7-binding protein 2	1	2	-0.07	-0.22	-0.15			
Q96EK4	THAP domain-containing protein 11	1	1	-0.06	-0.12	-0.08			
Q8WY91	THAP domain-containing protein 4	1	4	-0.23	-0.40	0.28			
Q9BU02	Thiamine-triphosphatase	2	7	-0.15	0.06	0.26			
P52888	Thimet oligopeptidase	8	26	-0.07	-0.09	0.05			
P51580	Thiopurine S-methyltransferase	4	9	0.04	0.22	0.30			
P10599	Thioredoxin	5	32	0.08	-0.03	0.35			
Q95881	Thioredoxin domain-containing protein 12	5	36	0.08	0.08	0.19			
Q9BRA2	Thioredoxin domain-containing protein 17	5	42	-0.12	-0.20	0.03			

Q8NBS9	Thioredoxin domain-containing protein 5	3	10	0.18	0.67	0.50			
O14530	Thioredoxin domain-containing protein 9	2	5	0.37	-0.04	-0.40			
Q16881	Thioredoxin reductase 1, cytoplasmic	13	60	-0.21	0.00	0.22			
Q9NNW7	Thioredoxin reductase 2, mitochondrial	8	21	0.13	-0.16	-0.21			
P30048	Thioredoxin-dependent peroxide reductase, mitochondrial	8	75	0.27	-0.11	-0.39			
O43396	Thioredoxin-like protein 1	9	47	-0.09	-0.03	0.07			
P83876	Thioredoxin-like protein 4A	2	11	-0.19	-0.33	-0.16			
Q9H3N1	Thioredoxin-related transmembrane protein 1	4	49	0.19	0.24	0.08			
Q9Y320	Thioredoxin-related transmembrane protein 2	2	2	-0.74	-0.15	0.59			
Q9H1E5	Thioredoxin-related transmembrane protein 4	2	17	0.41	0.56	-0.07		3	
Q16762	Thiosulfate sulfurtransferase	1	2	-0.82	0.08	0.90			
Q8NFU3	Thiosulfate sulfurtransferase/rhodanese-like domain-containing protein 1	6	47	-0.01	-0.39	-0.38			
Q96FV9	THO complex subunit 1	8	21	-0.06	-0.03	0.07			
Q8NI27	THO complex subunit 2	13	22	-0.14	-0.08	0.03			
Q96J01	THO complex subunit 3	2	2	-0.34	-0.08	0.25			
Q86V81	THO complex subunit 4	8	64	-0.34	-0.23	0.00			
Q13769	THO complex subunit 5 homolog	2	2	-0.04	-0.11	-0.06			
Q86W42	THO complex subunit 6 homolog	10	28	-0.11	-0.15	-0.07			
Q9NSU2	Three prime repair exonuclease 1	1	5	-0.48	-0.39	0.08			
Q9H6P5	Threonine aspartase 1	3	5	-0.09	-0.33	-0.32			
Q8IYQ7	Threonine synthase-like 1	1	6	0.39	-0.35	-0.89			4
P26639	Threonine--tRNA ligase, cytoplasmic	8	35	0.32	0.25	-0.05			
Q9BW92	Threonine--tRNA ligase, mitochondrial	3	4	-0.10	-0.26	-0.17			
P07996	Thrombospondin-1	15	56	-0.11	-0.12	0.05			
P24557	Thromboxane-A synthase	1	4	-0.75	0.13	0.79			3
Q9NXG2	THUMP domain-containing protein 1	11	51	0.02	-0.26	-0.15			
P19971	Thymidine phosphorylase	13	46	-0.15	0.35	0.36			
P23919	Thymidylate kinase	9	20	0.04	0.01	0.16			
Q9P016	Thymocyte nuclear protein 1	12	87	0.21	-0.82	-0.90		5	5
P63313	Thymosin beta-10	4	16	-0.06	-0.51	-0.14			
P62328	Thymosin beta-4	5	25	0.43	-0.27	-0.10			
Q9Y2W1	Thyroid hormone receptor-associated protein 3	22	146	-0.16	-0.15	0.07			
Q15643	Thyroid receptor-interacting protein 11	4	4	0.39	0.58	0.20			
Q9P031	Thyroid transcription factor 1-associated protein 26	2	5	0.30	-0.19	-0.50			
P05543	Thyroxine-binding globulin	1	1	0.56	0.95	0.40			
Q5JTD0	Tight junction-associated protein 1	3	5	0.34	0.11	-0.11			
O75663	TIP41-like protein	6	20	-0.07	0.05	0.07			
P04066	Tissue alpha-L-fucosidase	1	5	-0.54	-0.08	0.38			
Q8WZ42	Titin	2	10	0.81	0.13	-0.74	4		4
Q6P9B6	TLD domain-containing protein 1	1	4	-0.02	-0.03	0.00			
Q13077	TNF receptor-associated factor 1	2	2	-0.55	-0.31	0.25			
Q12933	TNF receptor-associated factor 2	3	5	-0.38	-0.28	0.09			
Q15025	TNFAIP3-interacting protein 1	2	14	-1.10	-0.80	0.31			
Q8NFZ5	TNFAIP3-interacting protein 2	1	2	-0.51	0.14	0.65			
Q9H0E2	Toll-interacting protein	4	14	-0.35	-0.05	0.21			
Q6ZVM7	TOM1-like protein 2	2	2	-0.09	-0.22	-0.14			
O14656	Torsin-1A	2	3	-0.18	0.24	0.33			
Q5JTV8	Torsin-1A-interacting protein 1	17	150	-0.08	0.24	0.22			
Q8NFQ8	Torsin-1A-interacting protein 2	1	1	0.29	0.33	0.02			
O14657	Torsin-1B	1	7	-0.42	0.13	0.60			5
Q5JU69	Torsin-2A	1	1	-0.97	-0.47	0.50			
Q9NXH8	Torsin-4A	2	8	-1.49	0.61	2.11	3	4	4
O94842	TOX high mobility group box family member 4	7	15	-0.10	0.02	0.15			
Q96S44	TP53-regulating kinase	5	27	-0.07	-0.01	-0.08			
O15050	TPR and ankyrin repeat-containing protein 1	5	14	0.02	0.29	0.25			
Q9H4I3	TraB domain-containing protein	1	11	-0.54	0.10	0.52			
Q92844	TRAF family member-associated NF-kappa-B activator	1	5	-0.06	0.33	0.26			
Q9UKE5	TRAF2 and NCK-interacting protein kinase	6	23	0.21	0.29	0.06			
Q9Y228	TRAF3-interacting JNK-activating modulator	18	113	-0.10	-0.22	-0.12			
P48553	Trafficking protein particle complex subunit 10	3	3	-0.24	0.17	0.42			
Q7Z392	Trafficking protein particle complex subunit 11	2	4	-0.29	-0.06	0.24			
Q8WVT3	Trafficking protein particle complex subunit 12	2	4	-0.15	0.10	0.26			
P0DI81	Trafficking protein particle complex subunit 2	1	1	-0.55	-0.14	0.39			
Q9UL33	Trafficking protein particle complex subunit 2-like protein	2	3	-0.27	0.15	0.34			
O43617	Trafficking protein particle complex subunit 3	4	9	-0.13	0.07	0.23			
Q9Y296	Trafficking protein particle complex subunit 4	2	4	-0.13	-0.04	0.03			
Q8IUR0	Trafficking protein particle complex subunit 5	2	3	-1.22	-0.38	0.82			
Q86S22	Trafficking protein particle complex subunit 6B	2	2	-0.68	-0.29	0.40			
Q9Y2L5	Trafficking protein particle complex subunit 8	2	2	-0.38	-0.29	0.09			
Q96Q05	Trafficking protein particle complex subunit 9	6	16	-0.23	0.07	0.33			
O14545	TRAF-type zinc finger domain-containing protein 1	4	12	-0.80	-0.23	0.42			
Q9BV79	Trans-2-enoyl-CoA reductase, mitochondrial	2	3	0.21	0.03	-0.17			
P37837	Transaldolase	20	259	0.10	-0.71	-0.92		5	5
P51532	Transcription activator BRG1	8	38	-0.08	-0.01	0.08			
Q9NPA8	Transcription and mRNA export factor ENY2	2	5	-0.32	-0.22	0.42			
P23193	Transcription elongation factor A protein 1	19	181	0.06	-0.20	-0.34			
O75764	Transcription elongation factor A protein 3	1	1	NA	NA	NA			
Q15170	Transcription elongation factor A protein-like 1	1	1	-0.38	0.53	0.93			
Q969E4	Transcription elongation factor A protein-like 3	8	15	-0.17	-0.43	-0.43			
Q15369	Transcription elongation factor B polypeptide 1	6	33	0.10	0.01	-0.10			
Q15370	Transcription elongation factor B polypeptide 2	6	29	-0.07	0.05	0.07			
P63272	Transcription elongation factor SPT4	2	4	0.10	0.05	-0.05			
O00267	Transcription elongation factor SPT5	19	65	-0.01	-0.07	-0.07			
Q7KZ85	Transcription elongation factor SPT6	18	42	-0.10	-0.02	-0.07			
O14776	Transcription elongation regulator 1	15	57	0.03	-0.33	-0.24			
Q9UGU0	Transcription factor 20	12	14	-0.04	-0.06	0.16			

Q7RTU1	Transcription factor 23	1	1	-0.19	-0.01	0.18			
Q9BQ70	Transcription factor 25	5	8	-0.29	0.09	0.43			
P36402	Transcription factor 7	3	17	-0.23	-0.62	-0.33		4	
Q00059	Transcription factor A, mitochondrial	8	29	0.39	-0.13	-0.66			4
P05412	Transcription factor AP-1	1	2	-0.59	0.05	0.65			
Q01664	Transcription factor AP-4	1	1	-0.46	-0.34	0.10			
P20290	Transcription factor BTF3	9	87	0.09	-0.13	-0.18			
Q96K17	Transcription factor BTF3 homolog 4	3	12	0.07	0.30	0.28			
Q16254	Transcription factor E2F4	3	4	-0.05	-0.45	-0.40			
Q66K89	Transcription factor E4F1	1	1	0.01	0.34	0.34			
P31629	Transcription factor HIVEP2	3	3	-0.25	-0.35	-0.10			
Q92994	Transcription factor IIB 90 kDa subunit	3	7	-0.30	-0.06	0.24			
P17275	Transcription factor jun-B	4	15	0.19	0.26	0.08			
P17535	Transcription factor jun-D	4	14	0.12	0.68	0.44		5	
Q9ULX9	Transcription factor MafF	2	12	-0.47	0.49	0.97			4
Q04206	Transcription factor p65	9	38	0.33	0.14	-0.19			
Q01201	Transcription factor RelB	5	9	0.09	0.16	0.13			
Q9Y651	Transcription factor SOX-21	1	3	-0.26	0.07	0.34			
P08047	Transcription factor Sp1	2	8	0.09	-0.05	0.10			
Q02086	Transcription factor Sp2	3	10	-0.39	-0.04	0.29			
Q02447	Transcription factor Sp3	3	17	-0.12	0.04	0.15			
Q02446	Transcription factor Sp4	2	5	0.13	0.58	0.49			
P52655	Transcription initiation factor IIA subunit 1	1	1	-0.06	0.04	0.11			
P52657	Transcription initiation factor IIA subunit 2	2	5	0.25	0.24	0.00			
Q00403	Transcription initiation factor IIB	10	33	0.12	-0.16	-0.21			
P29084	Transcription initiation factor IIE subunit beta	3	6	-0.24	-0.11	0.20			
P21675	Transcription initiation factor TFIID subunit 1	2	4	0.14	0.47	0.34			
Q12962	Transcription initiation factor TFIID subunit 10	4	17	-0.50	-0.20	0.28			
Q5VWG9	Transcription initiation factor TFIID subunit 3	2	4	0.03	-0.06	-0.09			
O00268	Transcription initiation factor TFIID subunit 4	12	41	-0.25	-0.05	0.20			
Q15542	Transcription initiation factor TFIID subunit 5	4	11	-0.12	-0.10	0.06			
P49848	Transcription initiation factor TFIID subunit 6	5	14	-0.32	-0.18	0.00			
Q15545	Transcription initiation factor TFIID subunit 7	1	1	-1.04	-0.62	0.43			
Q7Z7C8	Transcription initiation factor TFIID subunit 8	1	1	-0.11	-0.13	-0.01			
Q16594	Transcription initiation factor TFIID subunit 9	2	12	-0.26	-0.36	0.08			
Q9HBM6	Transcription initiation factor TFIID subunit 9B	2	6	-0.33	-0.32	0.02			
Q13263	Transcription intermediary factor 1-beta	25	280	-0.15	-0.30	-0.04			
Q9BYV9	Transcription regulator protein BACH2	1	3	-0.06	-0.10	-0.17			
Q15361	Transcription termination factor 1	1	1	-0.66	0.03	0.70			
Q00577	Transcriptional activator protein Pur-alpha	9	48	0.11	0.03	-0.08			
Q96QR8	Transcriptional activator protein Pur-beta	5	33	-0.20	0.19	0.33			
Q86TJ2	Transcriptional adapter 2-beta	1	65	-0.04	-0.14	-0.08			
O75528	Transcriptional adapter 3	1	2	NA	NA	NA			
P46100	Transcriptional regulator ATRX	14	29	-0.15	-0.06	0.01			
P49711	Transcriptional repressor CTCF	6	18	0.11	-0.07	-0.09			
Q12986	Transcriptional repressor NF-X1	1	1	-0.57	-0.04	0.51			
Q86YP4	Transcriptional repressor p66-alpha	23	159	-0.33	0.07	0.44			
Q8WXI9	Transcriptional repressor p66-beta	11	73	-0.12	-0.16	-0.07			
P25490	Transcriptional repressor protein YY1	11	32	-0.16	-0.21	-0.18			
Q96PN7	Transcriptional-regulating factor 1	3	5	-0.38	-0.23	0.16			
Q9Y4P3	Transducin beta-like protein 2	3	6	0.42	0.54	0.01		3	
Q12788	Transducin beta-like protein 3	7	11	0.20	-0.13	-0.33			
Q04724	Transducin-like enhancer protein 1	2	2	-0.36	0.00	0.36			
Q04726	Transducin-like enhancer protein 3	3	12	-0.08	-0.76	-0.80		5	4
Q9Y4A5	Transformation/transcription domain-associated protein	6	10	0.02	-0.20	-0.31			
Q13595	Transformer-2 protein homolog alpha	3	28	-0.18	-0.26	-0.06			
P62995	Transformer-2 protein homolog beta	6	65	-0.20	-0.43	-0.11			
O75410	Transforming acidic coiled-coil-containing protein 1	12	25	-0.07	0.10	0.18			
Q9Y6A5	Transforming acidic coiled-coil-containing protein 3	11	31	0.06	-0.58	-0.63		5	4
P01137	Transforming growth factor beta-1	2	2	-0.06	0.24	0.29			
Q8WUH2	Transforming growth factor-beta receptor-associated protein 1	2	5	-0.15	-0.09	-0.24			
P61586	Transforming protein RhoA	2	113	0.14	0.24	-0.02			
P37802	Transgelin-2	13	571	-0.18	0.00	0.36			
O43493	Trans-Golgi network integral membrane protein 2	4	5	0.16	0.00	-0.16			
Q9Y5S1	Transient receptor potential cation channel subfamily V member 2	4	11	-0.03	0.42	0.45		5	5
P55072	Transitional endoplasmic reticulum ATPase	46	504	0.04	0.12	0.12			
P29401	Transketolase	32	404	0.04	-0.45	-0.43			
Q14232	Translation initiation factor eIF-2B subunit alpha	3	9	-0.42	0.05	0.48			
P49770	Translation initiation factor eIF-2B subunit beta	5	5	0.34	0.07	-0.19			
Q9UI10	Translation initiation factor eIF-2B subunit delta	8	35	0.03	0.08	0.03			
Q13144	Translation initiation factor eIF-2B subunit epsilon	4	6	-0.13	0.02	0.21			
Q9NR50	Translation initiation factor eIF-2B subunit gamma	9	15	0.11	-0.06	-0.06			
P46199	Translation initiation factor IF-2, mitochondrial	4	7	0.23	-0.03	-0.31			
Q9H2K0	Translation initiation factor IF-3, mitochondrial	2	7	0.16	0.14	-0.01			
Q96EY4	Translation machinery-associated protein 16	2	2	-0.01	-0.07	-0.07			
Q9Y2S6	Translation machinery-associated protein 7	4	63	0.23	-0.53	-0.68		3	3
Q92616	Translational activator GCN1	36	113	0.44	0.24	-0.20			
Q9BSH4	Translational activator of cytochrome c oxidase 1	5	8	-0.05	-0.27	-0.02			
P13693	Translationally-controlled tumor protein	7	72	0.52	0.45	0.13			
Q15631	Translin	8	90	0.50	-0.08	-0.46			
Q99598	Translin-associated protein X	12	41	0.04	-0.28	-0.39			
Q99442	Translocation protein SEC62	3	10	0.71	0.33	-0.39		4	
Q9UGP8	Translocation protein SEC63 homolog	2	8	0.35	0.44	0.10			
P43307	Translocon-associated protein subunit alpha	3	16	0.52	0.40	-0.14			
P51571	Translocon-associated protein subunit delta	5	18	0.40	0.42	0.13			
Q9UNL2	Translocon-associated protein subunit gamma	1	5	0.16	0.45	0.18			

P48230	Transmembrane 4 L6 family member 4	1	4	NA	NA	NA			
Q9HD45	Transmembrane 9 superfamily member 3	2	7	0.07	0.38	0.26			
Q92544	Transmembrane 9 superfamily member 4	1	1	NA	NA	NA			
Q9UM00	Transmembrane and coiled-coil domain-containing protein 1	2	8	0.33	0.20	-0.07			
Q9ULS5	Transmembrane and coiled-coil domains protein 3	1	1	NA	NA	NA			
Q96BF3	Transmembrane and immunoglobulin domain-containing protein 2	1	9	0.02	0.52	0.51			
Q9BVT8	Transmembrane and ubiquitin-like domain-containing protein 1	1	2	0.04	0.07	0.03			
Q7Z403	Transmembrane channel-like protein 6	3	4	0.04	0.56	0.52			
P49755	Transmembrane emp24 domain-containing protein 10	7	44	0.44	0.62	-0.04		5	
Q15363	Transmembrane emp24 domain-containing protein 2	1	1	0.18	0.07	-0.13			
Q7Z7H5	Transmembrane emp24 domain-containing protein 4	2	26	-0.21	0.68	0.37		4	
Q9Y3A6	Transmembrane emp24 domain-containing protein 5	1	2	0.32	0.42	0.11			
Q9BVK6	Transmembrane emp24 domain-containing protein 9	2	22	-0.21	0.41	0.70			
Q9BVC6	Transmembrane protein 109	2	26	0.44	0.62	0.08		3	
P17152	Transmembrane protein 11, mitochondrial	1	1	NA	NA	NA			
Q9NX00	Transmembrane protein 160	1	2	0.06	-0.27	-0.32			
Q8IY95	Transmembrane protein 192	1	1	0.16	-1.19	-1.34			
Q9UHN6	Transmembrane protein 2	4	5	-0.74	-0.25	0.50			
Q6UW68	Transmembrane protein 205	1	1	0.35	0.47	0.11			
Q96SK2	Transmembrane protein 209	2	4	-0.04	0.09	0.24			
Q6NUQ4	Transmembrane protein 214	1	3	0.36	0.42	-0.02			
Q9HOR3	Transmembrane protein 222	1	1	NA	NA	NA			
Q96A57	Transmembrane protein 230	1	8	0.25	0.11	-0.19			
Q9H330	Transmembrane protein 245	1	9	-0.07	-0.57	-0.62		3	4
Q9BRR3	Transmembrane protein 246	1	1	-0.04	-0.06	-0.04			
P61165	Transmembrane protein 258	1	2	NA	NA	NA			
Q8WWA1	Transmembrane protein 40	1	1	-0.21	-0.14	0.06			
Q5BJD5	Transmembrane protein 41B	1	1	-0.14	-0.93	-0.78			
Q9BTV4	Transmembrane protein 43	9	35	0.47	0.41	0.25			
Q94886	Transmembrane protein 63A	1	1	1.20	1.24	0.02			
Q6UWD8	Transmembrane protein C16orf54	1	5	0.22	0.47	0.25			
Q6Z721	Transmembrane protein with metallophosphoesterase domain	1	1	-0.16	-0.06	0.11			
Q92973	Transportin-1	8	38	0.17	0.23	0.02			
Q13428	Treacle protein	43	266	0.40	0.24	-0.23			
P40939	Trifunctional enzyme subunit alpha, mitochondrial	40	333	0.21	0.12	-0.06			
P55084	Trifunctional enzyme subunit beta, mitochondrial	21	212	0.35	0.10	-0.24			
P22102	Trifunctional purine biosynthetic protein adenosine-3	26	81	0.21	-0.09	-0.33			
Q96RS0	Trimethylguanosine synthase	1	1	0.53	0.42	-0.10			
O15417	Trinucleotide repeat-containing gene 18 protein	1	2	-0.04	0.19	0.23			
Q9UPQ9	Trinucleotide repeat-containing gene 6B protein	5	9	0.02	0.09	0.09			
Q9HCJ0	Trinucleotide repeat-containing gene 6C protein	1	4	NA	NA	NA			
P60174	Triosephosphate isomerase	25	925	-0.23	-0.13	-0.03			
Q14142	Tripartite motif-containing protein 14	1	4	0.20	0.22	0.17			
Q12899	Tripartite motif-containing protein 26	3	4	0.10	0.32	0.28			
O00635	Tripartite motif-containing protein 38	4	7	0.02	-0.20	-0.33			
Q9C037	Tripartite motif-containing protein 4	3	4	-0.14	-0.01	0.14			
Q9C035	Tripartite motif-containing protein 5	2	2	-0.43	-0.11	0.31			
Q6PJ69	Tripartite motif-containing protein 65	5	10	0.27	0.20	0.03			
O14773	Tripeptidyl-peptidase 1	4	46	-0.47	0.10	0.42			
P29144	Tripeptidyl-peptidase 2	16	62	-0.04	-0.20	-0.15			
Q7Z2T5	TRMT1-like protein	1	3	0.15	-0.04	-0.19			
Q9UJA5	tRNA (adenine(58)-N(1))-methyltransferase non-catalytic subunit TRM6	4	10	-0.08	-0.22	-0.10			
Q9BV55	tRNA (adenine(58)-N(1))-methyltransferase, mitochondrial	1	1	0.08	-0.10	-0.17			
Q08J23	tRNA (cytosine(34)-C(5))-methyltransferase	22	104	-0.13	-0.10	-0.02			
Q9NXH9	tRNA (guanine(26)-N(2))-dimethyltransferase	6	11	0.02	-0.17	-0.48			
Q9UBP6	tRNA (guanine-N(7))-methyltransferase	1	2	-0.04	-0.40	-0.38			
P57081	tRNA (guanine-N(7))-methyltransferase non-catalytic subunit WDR4	1	2	-0.03	-0.21	-0.18			
Q9H3H1	tRNA dimethylallyltransferase, mitochondrial	1	1	0.56	0.24	-0.31			
Q9UI30	tRNA methyltransferase 112 homolog	4	26	0.18	-0.35	-0.64		5	
Q969Y2	tRNA modification GTPase GTPBP3, mitochondrial	4	6	0.08	-0.08	-0.09			
Q9Y606	tRNA pseudouridine synthase A, mitochondrial	4	13	0.27	-0.19	-0.56		4	
Q9NX07	tRNA selenocysteine 1-associated protein 1	2	4	0.17	0.15	-0.08			
Q6P1R4	tRNA-dihydrouridine(16/17) synthase-like	1	4	-0.08	-0.11	-0.04			
Q9NX74	tRNA-dihydrouridine(20) synthase-like	2	2	-0.47	-0.25	0.22			
Q9BUB4	tRNA-specific adenosine deaminase 1	1	2	0.30	0.44	0.14			
Q8WW01	tRNA-splicing endonuclease subunit Sen15	1	1	0.01	0.04	0.04			
Q9BSV6	tRNA-splicing endonuclease subunit Sen34	1	1	-0.71	-0.01	0.69			
Q7Z6J9	tRNA-splicing endonuclease subunit Sen54	1	2	0.21	-0.30	-0.50			
Q9Y3I0	tRNA-splicing ligase RtcB homolog	21	144	0.15	-0.22	-0.32			
Q9NZR1	Tropomodulin-2	2	10	0.68	0.08	-0.18	3		
Q9NYL9	Tropomodulin-3	14	115	-0.14	-0.09	0.07			
P09493	Tropomyosin alpha-1 chain	2	133	-0.82	-0.13	0.70			
P06753	Tropomyosin alpha-3 chain	6	337	-0.08	-0.19	0.07			
P67936	Tropomyosin alpha-4 chain	16	311	-0.52	-0.02	0.94	4		5
P23381	Tryptophan--tRNA ligase, cytoplasmic	11	66	0.02	0.17	0.10			
Q9UGM6	Tryptophan--tRNA ligase, mitochondrial	2	4	0.56	0.14	-0.33			
O75157	TSC22 domain family protein 2	3	5	0.24	0.23	0.00			
Q99576	TSC22 domain family protein 3	1	3	-0.10	-0.22	-0.33			
Q9Y3Q8	TSC22 domain family protein 4	8	37	-0.21	-0.08	0.01			
P49815	Tuberin	1	4	-0.36	-0.35	0.57			
P68363	Tubulin alpha-1B chain	1	462	0.24	1.58	1.33			
Q9BQE3	Tubulin alpha-1C chain	0	411	NA	NA	NA			
P68366	Tubulin alpha-4A chain	6	380	0.67	-0.14	-1.06	5		5
Q9NY65	Tubulin alpha-8 chain	1	134	-0.11	-0.13	-0.01			
P07437	Tubulin beta chain	5	979	-0.17	0.02	0.13			
Q9H4B7	Tubulin beta-1 chain	9	232	-0.15	-0.13	0.08			

Q13885	Tubulin beta-2A chain	1	784	0.33	-0.11	-0.44			
P04350	Tubulin beta-4A chain	3	739	0.33	0.20	-0.51			
P68371	Tubulin beta-4B chain	2	897	-0.12	0.26	0.50			
Q9BUF5	Tubulin beta-6 chain	2	328	-0.29	0.10	0.28			
P23258	Tubulin gamma-1 chain	4	18	-0.27	-0.36	-0.15			
Q99426	Tubulin-folding cofactor B	11	60	-0.33	-0.05	0.36			
O75347	Tubulin-specific chaperone A	10	70	-0.29	-0.23	0.09			
Q15814	Tubulin-specific chaperone C	3	4	-0.54	-0.45	0.09			
Q5QJ74	Tubulin-specific chaperone cofactor E-like protein	1	1	-0.71	-0.01	0.68			
Q9BTW9	Tubulin-specific chaperone D	3	9	-0.05	-0.20	-0.17			
Q14166	Tubulin-tyrosine ligase-like protein 12	5	25	0.21	0.00	-0.29			
Q9Y2W6	Tudor and KH domain-containing protein	2	6	0.25	0.30	0.05			
Q9H7E2	Tudor domain-containing protein 3	2	3	0.11	0.00	-0.12			
Q8NHU6	Tudor domain-containing protein 7	1	1	-0.16	0.34	0.50			
Q9UBB9	Tuftelin-interacting protein 11	6	17	-0.06	-0.05	0.04			
P21580	Tumor necrosis factor alpha-induced protein 3	8	16	0.52	0.74	0.10	4		5
O95379	Tumor necrosis factor alpha-induced protein 8	4	17	0.53	0.18	-0.34			
Q6P589	Tumor necrosis factor alpha-induced protein 8-like protein 2	2	4	-0.76	-0.38	0.39			
Q9Y275	Tumor necrosis factor ligand superfamily member 13B	1	3	-1.95	-1.49	0.46			
P20333	Tumor necrosis factor receptor superfamily member 1B	1	5	-0.26	1.59	1.85		3	4
O95407	Tumor necrosis factor receptor superfamily member 6B	1	2	NA	NA	NA			
Q15628	Tumor necrosis factor receptor type 1-associated DEATH domain protein	9	33	0.45	0.24	-0.24			
P55327	Tumor protein D52	8	34	-0.14	0.44	0.48		4	
O43399	Tumor protein D54	13	91	-0.20	-0.20	0.07			
O14683	Tumor protein p53-inducible protein 11	1	1	0.16	0.26	0.11			
Q12888	Tumor suppressor p53-binding protein 1	17	41	-0.08	-0.10	-0.15			
Q99816	Tumor susceptibility gene 101 protein	10	38	-0.17	0.31	0.43			
Q12792	Twinfilin-1	4	7	0.01	0.18	0.17			
Q6IB50	Twinfilin-2	15	99	-0.15	-0.07	0.07			
Q86T03	Type 1 phosphatidylinositol 4,5-bisphosphate 4-phosphatase	1	1	-0.19	-0.30	-0.11			
Q96PE3	Type I inositol 3,4-bisphosphate 4-phosphatase	12	38	-0.07	0.21	0.18			
P32019	Type II inositol 1,4,5-trisphosphate 5-phosphatase	1	1	0.12	0.48	0.34			
O15327	Type II inositol 3,4-bisphosphate 4-phosphatase	1	1	1.66	0.28	-1.37			
Q6RW13	Type-1 angiotensin II receptor-associated protein	1	4	-1.32	0.44	1.83	4		4
O43914	TYRO protein tyrosine kinase-binding protein	2	6	-2.00	0.52	2.50	3		3
P00519	Tyrosine-protein kinase ABL1	4	6	-0.16	0.01	0.45			
Q9UIG0	Tyrosine-protein kinase BAZ1B	26	82	0.13	-0.19	-0.29			
P51451	Tyrosine-protein kinase Blk	1	1	NA	NA	NA			
P41240	Tyrosine-protein kinase CSK	19	141	-0.41	0.01	0.38			
P07332	Tyrosine-protein kinase Fes/Fps	1	1	-3.81	1.41	5.23			
P06241	Tyrosine-protein kinase Fyn	4	21	0.15	0.60	0.48			
Q08881	Tyrosine-protein kinase ITK/TSK	1	1	-0.47	-0.88	-0.41			
P23458	Tyrosine-protein kinase JAK1	9	26	0.01	0.39	0.35			
P52333	Tyrosine-protein kinase JAK3	2	5	0.13	-0.17	-0.32			
P06239	Tyrosine-protein kinase Lck	13	94	0.53	0.16	-0.41			
P07948	Tyrosine-protein kinase Lyn	6	18	-1.02	0.38	1.36	4		4
Q86YV5	Tyrosine-protein kinase Sgk223	6	18	-0.34	-0.54	-0.56			
P43405	Tyrosine-protein kinase SYK	5	24	-0.83	0.00	0.89	3		3
P43403	Tyrosine-protein kinase ZAP-70	28	243	-0.52	0.29	0.83			4
P18031	Tyrosine-protein phosphatase non-receptor type 1	7	19	0.12	0.17	-0.09			
Q06124	Tyrosine-protein phosphatase non-receptor type 11	11	40	-0.02	0.04	-0.20			
Q05209	Tyrosine-protein phosphatase non-receptor type 12	14	45	-1.21	-0.08	1.19	5		5
Q12923	Tyrosine-protein phosphatase non-receptor type 13	1	1	NA	NA	NA			
Q99952	Tyrosine-protein phosphatase non-receptor type 18	5	30	-0.23	0.15	0.24			
P17706	Tyrosine-protein phosphatase non-receptor type 2	3	8	-0.31	0.18	0.54			
Q9Y2R2	Tyrosine-protein phosphatase non-receptor type 22	1	3	-0.02	0.56	0.53			
Q9H3S7	Tyrosine-protein phosphatase non-receptor type 23	11	20	0.06	0.03	-0.16			
P29074	Tyrosine-protein phosphatase non-receptor type 4	3	7	-0.75	0.61	1.55	3	5	5
P29350	Tyrosine-protein phosphatase non-receptor type 6	28	276	-0.32	-0.09	0.13			
P35236	Tyrosine-protein phosphatase non-receptor type 7	4	23	-0.16	0.08	0.10			
P43378	Tyrosine-protein phosphatase non-receptor type 9	2	8	-0.07	0.70	0.93		3	4
P54577	Tyrosine--tRNA ligase, cytoplasmic	27	132	-0.09	0.45	0.50			
Q9Y2Z4	Tyrosine--tRNA ligase, mitochondrial	4	6	0.08	-0.18	-0.28			
Q9NUW8	Tyrosyl-DNA phosphodiesterase 1	4	7	-0.07	-0.11	-0.19			
O95551	Tyrosyl-DNA phosphodiesterase 2	4	12	0.04	-0.25	-0.24			
P08621	U1 small nuclear ribonucleoprotein 70 kDa	17	99	-0.05	-0.23	-0.03			
P09012	U1 small nuclear ribonucleoprotein A	6	31	-0.17	-0.10	0.02			
P09234	U1 small nuclear ribonucleoprotein C	3	9	-0.05	-0.16	-0.11			
P09661	U2 small nuclear ribonucleoprotein A'	15	97	-0.08	-0.17	-0.10			
P08579	U2 small nuclear ribonucleoprotein B''	6	31	-0.17	0.03	0.19			
O15042	U2 snRNP-associated SURP motif-containing protein	15	64	-0.13	-0.30	-0.02			
Q9NV31	U3 small nucleolar ribonucleoprotein protein IMP3	1	2	0.70	-0.44	-1.14			
Q96G21	U3 small nucleolar ribonucleoprotein protein IMP4	2	3	-0.23	-0.23	-0.17			
O00566	U3 small nucleolar ribonucleoprotein protein MPP10	7	25	0.11	-0.19	-0.45			
Q9BVJ6	U3 small nucleolar RNA-associated protein 14 homolog A	17	38	0.16	-0.21	-0.41			
Q8TED0	U3 small nucleolar RNA-associated protein 15 homolog	2	5	0.26	-0.17	-0.32			
Q9Y5J1	U3 small nucleolar RNA-associated protein 18 homolog	8	29	0.33	-0.21	-0.52			4
Q9NYH9	U3 small nucleolar RNA-associated protein 6 homolog	3	3	0.14	-0.18	-0.32			
O43818	U3 small nucleolar RNA-interacting protein 2	5	12	0.08	-0.23	-0.33			
O43395	U4/U6 small nuclear ribonucleoprotein Prp3	13	30	-0.10	-0.16	0.05			
Q8WWY3	U4/U6 small nuclear ribonucleoprotein Prp31	11	66	-0.12	-0.18	-0.02			
O43172	U4/U6 small nuclear ribonucleoprotein Prp4	10	38	-0.21	-0.24	0.05			
Q8WVK2	U4/U6.U5 small nuclear ribonucleoprotein 27 kDa protein	3	4	-0.34	-0.19	0.06			
O43290	U4/U6.U5 tri-snRNP-associated protein 1	30	142	-0.16	-0.16	0.03			
Q53GS9	U4/U6.U5 tri-snRNP-associated protein 2	10	23	-0.32	-0.27	-0.01			
O75643	U5 small nuclear ribonucleoprotein 200 kDa helicase	35	179	-0.01	-0.04	0.00			

Q96D17	U5 small nuclear ribonucleoprotein 40 kDa protein	6	35	-0.23	-0.18	0.00			
O15116	U6 snRNA-associated Sm-like protein LSm1	2	12	-0.20	-0.03	0.06			
Q9Y333	U6 snRNA-associated Sm-like protein LSm2	7	41	-0.06	-0.25	-0.22			
P62310	U6 snRNA-associated Sm-like protein LSm3	4	41	-0.12	-0.17	-0.11			
Q9Y420	U6 snRNA-associated Sm-like protein LSm4	5	54	-0.25	-0.36	0.00			
Q9Y4Y9	U6 snRNA-associated Sm-like protein LSm5	1	1	0.25	0.02	-0.23			
P62312	U6 snRNA-associated Sm-like protein LSm6	6	34	-0.17	-0.43	-0.12			
Q9UK45	U6 snRNA-associated Sm-like protein LSm7	3	23	0.10	-0.14	-0.28			
P83369	U7 snRNA-associated Sm-like protein LSm11	1	1	NA	NA	NA			
Q96DE0	U8 snoRNA-decapping enzyme	1	2	0.77	0.25	-0.50			
Q96QD9	UAP56-interacting factor	10	35	-0.17	-0.13	0.00			
Q9NPG3	Ubinuclein-1	4	5	-0.35	-0.09	0.17			
Q6ZU65	Ubinuclein-2	1	1	0.96	0.13	-0.81			
Q9UMX0	Ubiquilin-1	3	56	0.06	0.06	-0.14			
Q9UHD9	Ubiquilin-2	4	38	0.34	-0.05	-0.83			
Q9NRR5	Ubiquilin-4	4	18	0.60	0.39	-0.27			
Q9BRT2	Ubiquinol-cytochrome-c reductase complex assembly factor 2	1	2	-0.14	0.20	0.35			
Q9Y2Z9	Ubiquinone biosynthesis monooxygenase COQ6	2	3	-0.14	-0.50	-0.38			
Q99807	Ubiquinone biosynthesis protein COQ7 homolog	4	12	-0.09	-0.52	-0.45			
O75208	Ubiquinone biosynthesis protein COQ9, mitochondrial	3	21	0.06	-0.35	-0.28			
Q14694	Ubiquitin carboxyl-terminal hydrolase 10	10	32	-0.09	-0.15	-0.07			
P51784	Ubiquitin carboxyl-terminal hydrolase 11	6	8	0.51	0.02	-0.24			
P54578	Ubiquitin carboxyl-terminal hydrolase 14	14	109	0.23	0.03	-0.21			
Q9Y4E8	Ubiquitin carboxyl-terminal hydrolase 15	7	13	0.27	0.22	-0.10			
O94966	Ubiquitin carboxyl-terminal hydrolase 19	3	5	-0.13	-0.03	-0.01			
Q9UPU5	Ubiquitin carboxyl-terminal hydrolase 24	12	21	0.03	-0.01	-0.19			
Q9UHP3	Ubiquitin carboxyl-terminal hydrolase 25	4	9	-0.21	-0.09	0.03			
Q96RU2	Ubiquitin carboxyl-terminal hydrolase 28	4	9	-0.62	0.20	0.70	5		5
Q9Y6I4	Ubiquitin carboxyl-terminal hydrolase 3	2	3	-0.10	0.11	0.20			
Q8TEY7	Ubiquitin carboxyl-terminal hydrolase 33	1	1	-1.45	-1.39	0.07			
Q9P275	Ubiquitin carboxyl-terminal hydrolase 36	1	4	0.42	0.14	-0.25			
Q13107	Ubiquitin carboxyl-terminal hydrolase 4	2	6	0.08	-0.19	-0.26			
Q96K76	Ubiquitin carboxyl-terminal hydrolase 47	24	79	0.10	0.03	0.12			
P45974	Ubiquitin carboxyl-terminal hydrolase 5	20	124	0.15	-0.25	-0.28			
Q93009	Ubiquitin carboxyl-terminal hydrolase 7	26	108	0.24	0.07	-0.10			
P40818	Ubiquitin carboxyl-terminal hydrolase 8	4	9	0.16	-0.01	-0.22			
Q9NQC7	Ubiquitin carboxyl-terminal hydrolase CYLD	6	15	0.02	0.04	0.04			
P15374	Ubiquitin carboxyl-terminal hydrolase isozyme L3	5	19	0.05	-0.09	-0.17			
Q9Y5K5	Ubiquitin carboxyl-terminal hydrolase isozyme L5	11	39	-0.04	0.10	0.09			
O95155	Ubiquitin conjugation factor E4 B	2	4	0.14	0.27	0.07			
O14562	Ubiquitin domain-containing protein UBFD1	2	3	-0.07	-0.12	-0.05			
Q92890	Ubiquitin fusion degradation protein 1 homolog	8	37	0.03	-0.03	0.08			
Q96FW1	Ubiquitin thioesterase OTUB1	11	47	0.14	0.02	-0.28			
Q96BN8	Ubiquitin thioesterase otulin	5	11	0.01	0.28	0.26			
O14933	Ubiquitin/ISG15-conjugating enzyme E2 L6	4	7	-0.45	0.12	0.17			
P62979	Ubiquitin-40S ribosomal protein S27a	13	509	-0.06	0.20	0.27			
P57075	Ubiquitin-associated and SH3 domain-containing protein A	2	4	0.52	-0.12	-0.65			
Q8TF42	Ubiquitin-associated and SH3 domain-containing protein B	1	1	0.00	-0.36	-0.35			
Q9BSL1	Ubiquitin-associated domain-containing protein 1	4	10	0.11	-0.09	-0.20			
Q8NBM4	Ubiquitin-associated domain-containing protein 2	1	3	-0.24	-0.23	0.38			
Q9NZ09	Ubiquitin-associated protein 1	3	11	0.29	0.50	0.25		5	
Q5T6F2	Ubiquitin-associated protein 2	7	10	-0.10	-0.04	0.12			
Q14157	Ubiquitin-associated protein 2-like	12	45	-0.01	-0.02	-0.01			
P51668	Ubiquitin-conjugating enzyme E2 D1	2	4	-0.12	0.14	0.31			
P61077	Ubiquitin-conjugating enzyme E2 D3	2	4	-0.06	-0.28	-0.22			
P61086	Ubiquitin-conjugating enzyme E2 K	5	22	0.04	-0.20	0.01			
P68036	Ubiquitin-conjugating enzyme E2 L3	8	44	0.03	0.19	0.17			
P61088	Ubiquitin-conjugating enzyme E2 N	6	101	0.35	0.03	-0.29			
Q9C0C9	Ubiquitin-conjugating enzyme E2 O	11	25	0.14	0.03	-0.09			
P49427	Ubiquitin-conjugating enzyme E2 R1	1	1	1.17	0.35	-0.81			
Q712K3	Ubiquitin-conjugating enzyme E2 R2	1	2	0.22	0.00	-0.22			
Q13404	Ubiquitin-conjugating enzyme E2 variant 1	3	57	0.11	-0.01	-0.22			
Q15819	Ubiquitin-conjugating enzyme E2 variant 2	4	67	-0.03	-0.10	-0.29			
Q8IX04	Ubiquitin-conjugating enzyme E2 variant 3	1	2	-0.40	0.53	0.92			
Q9H832	Ubiquitin-conjugating enzyme E2 Z	4	14	0.21	0.05	-0.22			
P61960	Ubiquitin-fold modifier 1	4	15	0.11	0.24	0.22			
Q9Y3C8	Ubiquitin-fold modifier-conjugating enzyme 1	2	22	-0.08	0.04	0.14			
Q8WVY7	Ubiquitin-like domain-containing CTD phosphatase 1	6	27	-0.23	-0.03	0.16			
P22314	Ubiquitin-like modifier-activating enzyme 1	43	522	0.09	-0.15	-0.24			
Q9GZ29	Ubiquitin-like modifier-activating enzyme 5	7	27	0.02	0.24	0.19			
A0AVT1	Ubiquitin-like modifier-activating enzyme 6	17	66	0.28	0.06	-0.20			
P41226	Ubiquitin-like modifier-activating enzyme 7	8	35	-0.33	0.00	0.26			
O95352	Ubiquitin-like modifier-activating enzyme ATG7	1	1	0.29	0.09	-0.20			
P11441	Ubiquitin-like protein 4A	6	13	0.07	-0.01	-0.16			
Q9BZL1	Ubiquitin-like protein 5	3	14	-0.24	-0.32	-0.08			
O94817	Ubiquitin-like protein ATG12	2	7	0.22	0.19	-0.25			
P05161	Ubiquitin-like protein ISG15	4	21	-0.46	0.17	0.67			
Q9NT62	Ubiquitin-like-conjugating enzyme ATG3	9	43	0.06	-0.11	-0.08			
Q05086	Ubiquitin-protein ligase E3A	12	33	0.06	-0.10	-0.08			
Q15386	Ubiquitin-protein ligase E3C	1	1	0.22	0.34	0.12			
Q04323	UBX domain-containing protein 1	8	20	-0.39	-0.21	0.20			
P68543	UBX domain-containing protein 2A	1	1	-0.40	0.31	0.72			
Q92575	UBX domain-containing protein 4	4	31	0.22	-0.11	-0.33			
Q9BZV1	UBX domain-containing protein 6	5	11	-0.02	0.15	0.18			
O94888	UBX domain-containing protein 7	2	17	-0.07	-0.18	-0.11			
Q9C0J1	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 4	1	4	0.19	-1.25	-1.43			

Q14376	UDP-glucose 4-epimerase	1	2	-0.54	0.28	0.83			
O60701	UDP-glucose 6-dehydrogenase	5	11	0.49	0.81	0.06		5	
Q9NYU2	UDP-glucose:glycoprotein glucosyltransferase 1	27	124	-0.02	0.21	0.19			
O15294	UDP-N-acetylglucosamine-peptide N-acetylglucosaminyltransferase 110 kD	12	27	0.01	-0.09	-0.13			
Q16222	UDP-N-acetylhexosamine pyrophosphorylase	2	7	0.10	0.31	0.25			
Q3KQV9	UDP-N-acetylhexosamine pyrophosphorylase-like protein 1	1	2	0.04	-0.52	-0.56			
Q6BDS2	UHRF1-binding protein 1	1	5	-0.13	0.17	0.31			
P30085	UMP-CMP kinase	10	66	-0.06	-0.08	0.07			
Q5EBM0	UMP-CMP kinase 2, mitochondrial	5	14	-0.25	0.14	0.39			
Q6ZUT1	Uncharacterized protein C11orf57	1	1	-0.06	0.14	0.21			
Q96C57	Uncharacterized protein C12orf43	5	12	0.02	0.09	-0.11			
Q9BXV9	Uncharacterized protein C14orf142	4	28	0.01	-0.04	-0.03			
Q8NEP4	Uncharacterized protein C17orf47	1	1	-0.67	0.05	0.73			
Q96GS4	Uncharacterized protein C17orf59	11	44	-0.08	0.05	0.47			
Q9BQA9	Uncharacterized protein C17orf62	2	7	-0.47	0.28	0.75			
Q9BSJ5	Uncharacterized protein C17orf80	1	1	0.76	-0.38	-1.14			
Q53F19	Uncharacterized protein C17orf85	9	37	-0.34	-0.07	0.26			
A11188	Uncharacterized protein C17orf89	1	1	-0.37	-0.17	0.18			
Q96B23	Uncharacterized protein C18orf25	1	1	-0.81	-0.71	0.10			
Q96DM3	Uncharacterized protein C18orf8	2	3	-0.18	0.13	0.37			
Q9BQ61	Uncharacterized protein C19orf43	5	24	-0.19	-0.01	0.35			
Q8N9M1	Uncharacterized protein C19orf47	3	4	-0.51	-0.08	0.43			
Q9BSF4	Uncharacterized protein C19orf52	2	4	0.02	-0.07	-0.01			
Q9NX04	Uncharacterized protein C1orf109	1	1	NA	NA	NA			
Q6ZSJ8	Uncharacterized protein C1orf122	1	1	-0.22	0.08	0.27			
Q8NDD1	Uncharacterized protein C1orf131	2	2	-0.10	0.17	0.28			
Q9BV19	Uncharacterized protein C1orf50	1	4	-0.23	-0.29	-0.02			
Q8WWC4	Uncharacterized protein C2orf47, mitochondrial	1	3	0.27	0.00	-0.33			
Q6NW34	Uncharacterized protein C3orf17	1	1	-0.32	-0.15	0.18			
Q8N8J7	Uncharacterized protein C4orf32	1	1	0.95	-0.03	-0.98			
Q9P0P8	Uncharacterized protein C6orf203	1	1	NA	NA	NA			
Q9BRJ6	Uncharacterized protein C7orf50	6	15	0.16	-0.27	-0.49			
Q5T280	Uncharacterized protein C9orf114	3	10	-0.14	-0.08	0.08			
Q9BUH6	Uncharacterized protein C9orf142	13	193	0.11	0.38	0.30		5	
Q9NZ63	Uncharacterized protein C9orf78	9	17	0.00	-0.33	-0.41			
Q8TB03	Uncharacterized protein CXorf38	1	3	-0.06	-0.01	0.05			
Q6ZSR9	Uncharacterized protein FLJ45252	12	71	0.14	0.08	-0.04			
Q6ZRH9	Uncharacterized protein FLJ46347	1	7	0.39	-0.17	-0.38			
Q96AT1	Uncharacterized protein KIAA1143	7	22	-0.31	0.00	-0.04			
Q9P2H0	Uncharacterized protein KIAA1377	1	1	-0.63	-0.11	0.53			
Q9HCM1	Uncharacterized protein KIAA1551	1	2	-0.38	-0.39	-0.01			
Q9BY89	Uncharacterized protein KIAA1671	1	1	-0.91	-0.66	0.27			
Q5JYT7	Uncharacterized protein KIAA1755	1	5	0.03	0.25	0.13			
O00160	Unconventional myosin-IIf	29	154	-0.13	1.39	1.32		5	5
B011T2	Unconventional myosin-Ig	36	262	0.02	0.59	0.36		4	
Q13459	Unconventional myosin-IXb	16	52	-0.35	-0.03	0.21			
Q9Y4I1	Unconventional myosin-Va	7	12	0.29	0.54	0.20		5	
Q9UM54	Unconventional myosin-VI	1	1	0.29	0.42	0.14			
Q92614	Unconventional myosin-XVIIIa	38	93	0.12	0.40	0.32		4	
O94763	Unconventional prefoldin RPB5 interactor 1	2	4	0.12	-0.16	-0.16			
Q14146	Unhealthy ribosome biogenesis protein 2 homolog	1	2	0.82	0.12	-0.69			
Q9HB07	UPF0160 protein MYG1, mitochondrial	4	17	0.01	-0.10	-0.13			
Q9BSU1	UPF0183 protein C16orf70	1	2	-0.31	0.02	0.31			
Q8WUR7	UPF0235 protein C15orf40	1	6	0.13	-0.11	-0.28			
Q7Z3D6	UPF0317 protein C14orf159, mitochondrial	4	20	0.50	0.35	-0.07		5	
Q9H993	UPF0364 protein C6orf211	3	12	0.10	0.22	0.22			
Q96GQ5	UPF0420 protein C16orf58	1	1	0.02	-0.06	-0.07			
Q9H5V9	UPF0428 protein CXorf56	4	10	-0.20	-0.19	-0.01			
Q8WUH6	UPF0444 transmembrane protein C12orf23	5	32	-0.02	-0.28	-0.22			
Q9UFG5	UPF0449 protein C19orf25	3	5	-0.18	-0.19	0.11			
Q7Z6I8	UPF0461 protein C5orf24	2	3	-0.70	0.05	0.75			
Q9Y6A4	UPF0468 protein C16orf80	2	2	-0.12	-0.15	-0.03			
Q7Z7F0	UPF0469 protein KIAA0907	2	2	-0.29	0.21	0.51			
Q9H7E9	UPF0488 protein C8orf33	5	12	0.03	-0.19	-0.30			
Q49AR2	UPF0489 protein C5orf22	2	6	0.00	0.01	-0.08			
Q9P2B7	UPF0501 protein KIAA1430	1	1	0.03	0.03	-0.02			
Q7Z3J2	UPF0505 protein C16orf62	1	4	0.15	0.16	-0.01			
Q9NUL5	UPF0515 protein C19orf66	3	21	-0.05	0.25	0.32			
Q6NTE8	UPF0544 protein C5orf45	1	1	-0.14	-0.41	-0.26			
Q5T6V5	UPF0553 protein C9orf64	3	14	-0.07	-0.22	0.01			
Q969H8	UPF0556 protein C19orf10	5	23	-0.65	-0.19	0.36		3	
Q2NKX9	UPF0561 protein C2orf68	1	2	-0.32	0.19	0.52			
Q8N8R5	UPF0565 protein C2orf69	1	1	0.00	-0.10	-0.10			
Q9Y224	UPF0568 protein C14orf166	11	101	0.21	0.01	-0.17			
Q96S19	UPF0585 protein C16orf13	5	9	-0.08	-0.22	-0.07			
Q9NWW4	UPF0587 protein C1orf123	7	23	-0.31	0.00	-0.06			
Q6P1X6	UPF0598 protein C8orf82	1	1	NA	NA	NA			
Q9NWW4	UPF0609 protein C4orf27	3	6	-0.19	-0.10	0.02			
Q5T2E6	UPF0668 protein C10orf76	1	1	-0.01	-0.03	-0.01			
Q9GZN8	UPF0687 protein C20orf27	1	1	-0.05	-0.32	-0.27			
Q8IYL3	UPF0688 protein C1orf174	4	19	-0.53	-0.33	0.37			
Q8N6N3	UPF0690 protein C1orf52	1	8	-0.21	-0.06	0.14			
Q96B45	UPF0693 protein C10orf32	5	17	-0.22	0.13	0.22			
Q9H3H3	UPF0696 protein C11orf68	4	8	0.16	0.15	-0.07			
P57076	UPF0769 protein C21orf59	1	7	0.20	-0.16	-0.31			
Q96IX5	Up-regulated during skeletal muscle growth protein 5	2	5	0.41	0.20	-0.01			

P22415	Upstream stimulatory factor 1	2	4	-0.01	0.28	0.28			
Q15853	Upstream stimulatory factor 2	1	7	-0.04	0.04	0.15			
Q9NZ17	Upstream-binding protein 1	2	6	-0.02	0.15	0.14			
Q96BW1	Uracil phosphoribosyltransferase homolog	1	2	-0.48	0.29	0.78			
P13051	Uracil-DNA glycosylase	2	3	0.11	0.29	0.17			
P11172	Uridine 5'-monophosphate synthase	7	17	0.08	-0.07	-0.43			
Q16831	Uridine phosphorylase 1	3	13	-0.25	0.50	0.68			
Q9NWZ5	Uridine-cytidine kinase-like 1	1	1	0.42	0.25	-0.17			
P06132	Uroporphyrinogen decarboxylase	1	2	0.44	0.15	-0.29			
P10746	Uroporphyrinogen-III synthase	2	3	-0.04	0.04	0.08			
Q16851	UTP--glucose-1-phosphate uridylyltransferase	27	134	0.16	-0.22	-0.40			
P46939	Utrophin	25	56	-0.37	0.29	0.69			3
P54725	UV excision repair protein RAD23 homolog A	3	31	0.32	0.06	-0.06			
P54727	UV excision repair protein RAD23 homolog B	12	98	-0.08	0.08	0.18			
Q9P2Y5	UV radiation resistance-associated gene protein	1	1	-0.19	0.38	0.58			
P86790	Vacuolar fusion protein CCZ1 homolog B	3	3	0.05	0.09	0.04			
Q7L1V2	Vacuolar fusion protein MON1 homolog B	1	2	-0.19	-0.07	0.11			
Q9H270	Vacuolar protein sorting-associated protein 11 homolog	4	12	-0.18	0.13	0.29			
Q96RL7	Vacuolar protein sorting-associated protein 13A	2	3	-0.06	-0.33	-0.27			
Q709C8	Vacuolar protein sorting-associated protein 13C	24	88	0.48	0.21	-0.28			
Q5THJ4	Vacuolar protein sorting-associated protein 13D	1	1	0.39	0.20	-0.18			
Q9H269	Vacuolar protein sorting-associated protein 16 homolog	5	21	-0.20	0.02	0.26			
Q9P253	Vacuolar protein sorting-associated protein 18 homolog	5	8	-0.01	0.12	0.24			
O75436	Vacuolar protein sorting-associated protein 26A	3	10	0.29	0.08	0.06			
Q4G0F5	Vacuolar protein sorting-associated protein 26B	7	28	-0.22	0.15	0.36			
Q9UK41	Vacuolar protein sorting-associated protein 28 homolog	2	4	-0.36	0.13	0.46			
Q9UBQ0	Vacuolar protein sorting-associated protein 29	9	44	0.05	0.12	0.00			
Q96AX1	Vacuolar protein sorting-associated protein 33A	3	5	-0.24	-0.01	0.23			
Q9H267	Vacuolar protein sorting-associated protein 33B	4	7	-0.03	0.02	-0.02			
Q96QK1	Vacuolar protein sorting-associated protein 35	11	47	0.00	0.11	0.05			
Q8NEZ2	Vacuolar protein sorting-associated protein 37A	2	3	0.14	0.22	0.07			
Q9H9H4	Vacuolar protein sorting-associated protein 37B	4	25	-0.32	0.30	0.68			5
Q86XT2	Vacuolar protein sorting-associated protein 37D	1	5	NA	NA	NA			
P49754	Vacuolar protein sorting-associated protein 41 homolog	1	1	-0.09	0.21	0.30			
Q9NRW7	Vacuolar protein sorting-associated protein 45	3	6	-0.22	-0.03	0.14			
Q9UN37	Vacuolar protein sorting-associated protein 4A	5	57	-0.03	-0.11	0.02			
O75351	Vacuolar protein sorting-associated protein 4B	14	80	-0.18	0.10	0.30			
Q9UID3	Vacuolar protein sorting-associated protein 51 homolog	5	8	0.09	0.04	-0.01			
Q8N1B4	Vacuolar protein sorting-associated protein 52 homolog	6	13	-0.02	0.00	0.02			
Q5VIR6	Vacuolar protein sorting-associated protein 53 homolog	1	1	0.10	0.12	0.03			
Q15906	Vacuolar protein sorting-associated protein 72 homolog	1	1	-0.91	-0.07	0.85			
Q8N3P4	Vacuolar protein sorting-associated protein 8 homolog	2	3	-0.10	-0.17	-0.08			
Q9NP79	Vacuolar protein sorting-associated protein VTA1 homolog	3	16	0.09	0.06	-0.06			
Q9BRG1	Vacuolar protein-sorting-associated protein 25	2	7	-0.25	-0.03	0.12			
Q86VN1	Vacuolar protein-sorting-associated protein 36	6	16	-0.28	-0.03	0.28			
Q96H20	Vacuolar-sorting protein SNF8	5	15	-0.15	-0.03	0.17			
P26640	Valine--tRNA ligase	25	163	0.31	0.15	-0.20			
Q55T30	Valine--tRNA ligase, mitochondrial	2	3	-0.03	-0.07	-0.02			
Q96JC1	Vam6/Vps39-like protein	3	5	0.03	0.19	0.28			
Q14119	Vascular endothelial zinc finger 1	3	7	0.00	0.07	0.11			
P50552	Vasodilator-stimulated phosphoprotein	21	222	-0.65	-0.09	0.52	5		5
P49748	Very long-chain specific acyl-CoA dehydrogenase, mitochondrial	22	121	0.19	0.26	0.09			
Q6Y1H2	Very-long-chain (3R)-3-hydroxyacyl-[acyl-carrier protein] dehydratase 2	1	3	0.54	0.42	-0.13			
Q9P035	Very-long-chain (3R)-3-hydroxyacyl-[acyl-carrier protein] dehydratase 3	2	3	0.26	0.13	-0.12			
Q9NZ01	Very-long-chain enoyl-CoA reductase	2	2	0.30	0.14	-0.16			
Q9Y3E0	Vesicle transport protein GOT1B	1	1	-0.10	0.38	0.49			
Q12981	Vesicle transport protein SEC20	2	2	0.96	0.47	-0.48			
O95562	Vesicle transport protein SFT2B	1	2	NA	NA	NA			
Q96AJ9	Vesicle transport through interaction with t-SNAREs homolog 1A	1	2	-1.67	-0.73	0.95			
Q9UEU0	Vesicle transport through interaction with t-SNAREs homolog 1B	7	12	-0.24	-0.05	0.18			
P63027	Vesicle-associated membrane protein 2	2	21	-0.01	0.01	0.01			
Q15836	Vesicle-associated membrane protein 3	1	8	-0.21	0.38	0.57			
O75379	Vesicle-associated membrane protein 4	1	1	-0.21	-0.04	0.18			
O95183	Vesicle-associated membrane protein 5	1	13	0.13	0.27	0.13			
Q9BV40	Vesicle-associated membrane protein 8	4	40	-0.50	0.45	0.98			4
Q9P0L0	Vesicle-associated membrane protein-associated protein A	6	33	0.04	0.16	0.14			
O95292	Vesicle-associated membrane protein-associated protein B/C	6	24	0.00	0.08	0.03			
P46459	Vesicle-fusing ATPase	19	78	0.08	0.02	-0.08			
O75396	Vesicle-trafficking protein SEC22b	12	115	0.31	0.20	0.13			
Q12907	Vesicular integral-membrane protein VIP36	7	26	0.20	0.37	0.42			
Q00341	Vigilin	15	28	0.24	0.33	0.12		5	
P08670	Vimentin	53	2133	0.82	0.01	-0.89	5		5
P18206	Vinculin	72	625	-0.28	0.49	0.89		5	5
Q9H0V9	VIP36-like protein	1	3	0.34	0.45	0.05			
P02774	Vitamin D-binding protein	2	3	1.48	1.46	-0.02			
P04004	Vitronection	1	1	0.94	0.65	-0.28			
P21796	Voltage-dependent anion-selective channel protein 1	20	196	0.08	0.27	0.26			
P45880	Voltage-dependent anion-selective channel protein 2	12	143	-0.06	0.23	0.11			
Q9Y277	Voltage-dependent anion-selective channel protein 3	11	93	0.05	0.15	-0.12			
Q9NY47	Voltage-dependent calcium channel subunit alpha-2/delta-2	7	14	0.76	1.47	0.62	3		3
Q96D96	Voltage-gated hydrogen channel 1	2	2	-1.21	0.02	1.23			
Q13303	Voltage-gated potassium channel subunit beta-2	16	91	-0.13	0.29	0.39			
P04275	von Willebrand factor	2	8	0.03	-0.42	-0.53			
O00534	von Willebrand factor A domain-containing protein 5A	5	6	-0.71	-0.77	0.15			
A3KMH1	von Willebrand factor A domain-containing protein 8	13	25	0.66	0.36	-0.34	5		
Q9Y487	V-type proton ATPase 116 kDa subunit a isoform 2	1	1	-0.08	0.27	0.36			

Q13488	V-type proton ATPase 116 kDa subunit a isoform 3	2	3	-0.63	0.00	0.63			
P38606	V-type proton ATPase catalytic subunit A	13	94	-0.10	-0.04	0.13			
P21281	V-type proton ATPase subunit B, brain isoform	17	86	-0.10	-0.03	-0.04			
P21283	V-type proton ATPase subunit C 1	6	15	-0.20	0.19	0.29			
Q9Y5K8	V-type proton ATPase subunit D	3	7	-0.18	-0.11	0.06			
P61421	V-type proton ATPase subunit d 1	1	3	0.15	0.55	0.56			
P36543	V-type proton ATPase subunit E 1	9	44	-0.22	-0.16	0.18			
O75348	V-type proton ATPase subunit G 1	3	10	-0.01	-0.05	0.08			
Q9UI12	V-type proton ATPase subunit H	4	21	-0.08	-0.06	0.08			
Q15904	V-type proton ATPase subunit S1	1	2	0.03	-0.04	-0.08			
Q9NQA3	WAS protein family homolog 6	1	14	-0.33	-0.48	-0.15			
O43516	WAS/WASL-interacting protein family member 1	15	175	-0.34	0.17	0.50			5
Q2M389	WASH complex subunit 7	4	12	0.01	-0.19	-0.20			
Q9Y3C0	WASH complex subunit CCDC53	1	1	NA	NA	NA			
Q5SNT6	WASH complex subunit FAM21B	3	31	-0.21	-0.04	0.18			
Q9Y4E1	WASH complex subunit FAM21C	3	31	-0.05	-0.12	-0.07			
Q12768	WASH complex subunit strumpellin	1	4	-0.04	0.06	0.10			
Q8IWB7	WD repeat and FYVE domain-containing protein 1	1	1	-0.17	0.26	0.43			
Q9Y4P8	WD repeat domain phosphoinositide-interacting protein 2	2	3	0.13	-0.13	-0.17			
Q9Y484	WD repeat domain phosphoinositide-interacting protein 4	2	2	0.11	0.36	0.24			
O75083	WD repeat-containing protein 1	37	573	-0.22	-0.20	0.10			
Q9BZH6	WD repeat-containing protein 11	1	2	-0.24	0.25	0.49			
Q9H1Z4	WD repeat-containing protein 13	2	6	-0.22	0.16	0.36			
Q9BV38	WD repeat-containing protein 18	2	12	0.18	-0.28	-0.46			
Q96S15	WD repeat-containing protein 24	1	10	0.12	-0.29	-0.30			
Q9H7D7	WD repeat-containing protein 26	3	4	0.13	0.28	0.16			
Q9UNX4	WD repeat-containing protein 3	4	6	-0.08	0.00	0.01			
Q8NI36	WD repeat-containing protein 36	6	12	0.43	-0.09	-0.53			4
Q9Y2I8	WD repeat-containing protein 37	15	55	-0.09	-0.02	0.09			
Q15061	WD repeat-containing protein 43	3	22	0.22	-0.31	-0.57			4
Q5JSJ3	WD repeat-containing protein 44	16	41	0.11	0.00	0.01			
O15213	WD repeat-containing protein 46	10	15	0.23	-0.18	-0.36			
Q8TAF3	WD repeat-containing protein 48	1	1	-0.30	0.29	0.57			
P61964	WD repeat-containing protein 5	4	23	0.14	0.04	-0.12			
Q9H6Y2	WD repeat-containing protein 55	4	5	-0.01	0.06	0.03			
Q6PJ19	WD repeat-containing protein 59	1	1	0.85	-0.21	-1.08			
Q9GZS3	WD repeat-containing protein 61	8	29	0.16	0.00	-0.13			
Q9Y4E6	WD repeat-containing protein 7	1	7	-0.91	-0.95	0.08			3
Q9NW82	WD repeat-containing protein 70	5	19	-0.09	0.01	0.06			
Q6P4I2	WD repeat-containing protein 73	1	1	-0.04	0.05	0.09			
Q6RFH5	WD repeat-containing protein 74	3	10	0.14	-0.18	-0.30			
Q8IWA0	WD repeat-containing protein 75	1	1	0.34	0.19	-0.15			
Q562E7	WD repeat-containing protein 81	6	22	0.23	-0.02	-0.28			
Q6UXN9	WD repeat-containing protein 82	9	26	-0.01	0.06	0.10			
Q96FK6	WD repeat-containing protein 89	4	5	0.13	-0.33	-0.40			
A4D1P6	WD repeat-containing protein 91	6	23	0.20	0.04	-0.33			
Q96MX6	WD repeat-containing protein 92	4	8	0.17	-0.18	-0.49			
Q9NXC5	WD repeat-containing protein mio	5	12	0.21	-0.06	-0.25			
Q2TAY7	WD40 repeat-containing protein SMU1	12	98	-0.07	-0.14	-0.11			
Q14191	Werner syndrome ATP-dependent helicase	1	1	-0.12	-0.34	-0.21			
Q96I51	Williams-Beuren syndrome chromosomal region 16 protein	1	4	0.14	-0.16	-0.13			
Q7Z5K2	Wings apart-like protein homolog	10	19	0.02	-0.14	-0.04			
P42768	Wiskott-Aldrich syndrome protein	19	245	-0.36	0.09	0.48			5
Q9Y6W5	Wiskott-Aldrich syndrome protein family member 2	10	57	-0.07	0.26	0.51			4
O76024	Wolframin	2	4	-0.09	0.36	0.45			
Q9Y2W2	WW domain-binding protein 11	17	106	-0.28	-0.23	0.00			
Q969T9	WW domain-binding protein 2	3	7	-0.23	-0.43	-0.29			
O75554	WW domain-binding protein 4	1	1	-0.20	-0.53	-0.34			
Q9NQW7	Xaa-Pro aminopeptidase 1	9	28	-0.39	0.12	0.30			
P12955	Xaa-Pro dipeptidase	10	48	0.17	0.36	0.22			
P13010	X-ray repair cross-complementing protein 5	36	414	0.16	-0.18	-0.40			5
P12956	X-ray repair cross-complementing protein 6	36	532	0.23	-0.23	-0.41			5
Q92536	Y+L amino acid transporter 2	1	3	0.24	0.33	0.09			
P16989	Y-box-binding protein 3	3	16	-0.20	-1.01	-1.23			
Q9ULM3	YEATS domain-containing protein 2	1	1	0.82	0.41	-0.39			
Q95619	YEATS domain-containing protein 4	2	9	-0.32	-0.41	0.05			
P49750	YLP motif-containing protein 1	16	53	-0.21	-0.25	0.00			
Q86U90	YrdC domain-containing protein, mitochondrial	1	1	-1.43	-0.33	1.09			
Q9BYJ9	YTH domain family protein 1	2	8	0.00	-0.25	-0.25			
Q9Y5A9	YTH domain family protein 2	2	11	0.02	0.01	0.04			
Q7Z739	YTH domain family protein 3	5	15	-0.32	-0.09	0.19			
Q96MU7	YTH domain-containing protein 1	2	4	0.01	-0.20	-0.21			
Q8IY57	YY1-associated factor 2	1	3	-0.05	0.42	0.48			
Q9H171	Z-DNA-binding protein 1	7	13	-0.59	-0.11	0.59			
O95625	Zinc finger and BTB domain-containing protein 11	3	3	-0.27	0.01	0.28			
Q8N680	Zinc finger and BTB domain-containing protein 2	2	4	-0.14	-0.10	0.19			
Q9ULJ3	Zinc finger and BTB domain-containing protein 21	2	2	-0.16	-0.02	0.14			
Q9P1Z0	Zinc finger and BTB domain-containing protein 4	4	10	0.01	-0.05	-0.16			
O95365	Zinc finger and BTB domain-containing protein 7A	1	8	-0.17	-0.20	-0.14			
O96006	Zinc finger BED domain-containing protein 1	1	2	-0.12	0.06	0.19			
O60293	Zinc finger C3H1 domain-containing protein	2	4	-0.96	-0.56	0.41			
Q96K80	Zinc finger CCCH domain-containing protein 10	1	1	-0.30	0.04	0.35			
O75152	Zinc finger CCCH domain-containing protein 11A	26	74	-0.23	-0.22	-0.06			
Q5T200	Zinc finger CCCH domain-containing protein 13	3	11	-0.15	-0.07	0.07			
Q6PJT7	Zinc finger CCCH domain-containing protein 14	11	34	-0.08	0.01	0.09			
Q8WU90	Zinc finger CCCH domain-containing protein 15	7	23	0.37	0.04	-0.46			

Q86VM9	Zinc finger CCCH domain-containing protein 18	10	25	-0.28	-0.20	-0.14			
Q8IXZ2	Zinc finger CCCH domain-containing protein 3	1	1	0.14	-0.30	-0.44			
Q9UPT8	Zinc finger CCCH domain-containing protein 4	15	68	-0.17	-0.21	-0.01			
Q8N5P1	Zinc finger CCCH domain-containing protein 8	2	3	-0.18	-0.55	-0.02			
Q7Z2W4	Zinc finger CCCH-type antiviral protein 1	22	127	0.07	-0.09	-0.14			
Q96H79	Zinc finger CCCH-type antiviral protein 1-like	1	1	0.35	0.38	0.04			
Q8N5A5	Zinc finger CCCH-type with G patch domain-containing protein	11	24	-0.15	-0.24	-0.05			
Q8TBK6	Zinc finger CCHC domain-containing protein 10	1	5	-0.22	-0.04	0.15			
Q8N3Z6	Zinc finger CCHC domain-containing protein 7	1	1	-0.02	-0.17	-0.17			
Q6NZY4	Zinc finger CCHC domain-containing protein 8	10	46	-0.07	-0.06	0.02			
Q8N567	Zinc finger CCHC domain-containing protein 9	2	2	0.09	0.00	-0.09			
Q8TBF4	Zinc finger CCHC-type and RNA-binding motif-containing protein 1	1	1	-0.02	0.09	0.12			
Q96K21	Zinc finger FYVE domain-containing protein 19	2	12	-0.37	-0.08	0.27			
Q9UHR6	Zinc finger HIT domain-containing protein 2	2	2	-0.17	0.05	0.22			
Q96NC0	Zinc finger matrix-type protein 2	2	6	-0.27	-0.38	0.03			
Q9UDW3	Zinc finger matrix-type protein 5	1	1	-0.19	-0.09	0.11			
Q14202	Zinc finger MYM-type protein 3	1	1	NA	NA	NA			
Q15326	Zinc finger MYND domain-containing protein 11	2	4	-0.19	0.09	0.30			
P52739	Zinc finger protein 131	1	1	-0.07	0.00	0.05			
P52740	Zinc finger protein 132	2	2	-0.07	0.04	0.09			
P52747	Zinc finger protein 143	4	12	-0.04	0.21	0.22			
Q9UQR1	Zinc finger protein 148	9	23	-0.25	-0.09	-0.05			
Q15697	Zinc finger protein 174	1	2	NA	NA	NA			
O15231	Zinc finger protein 185	1	1	-0.09	-0.18	-0.11			
O43670	Zinc finger protein 207	3	22	-0.04	-0.22	-0.03			
O75362	Zinc finger protein 217	1	1	-0.58	-0.21	0.38			
P17026	Zinc finger protein 22	7	20	-0.08	-0.26	-0.26			
P17028	Zinc finger protein 24	3	4	0.11	0.06	0.03			
Q8N554	Zinc finger protein 276	7	20	-0.27	-0.29	0.06			
A6NFI3	Zinc finger protein 316	2	3	0.09	-0.04	-0.14			
Q5VUA4	Zinc finger protein 318	1	2	-0.20	0.03	0.23			
P17041	Zinc finger protein 32	1	3	-0.45	-0.05	0.41			
Q9Y3S2	Zinc finger protein 330	1	1	-0.99	-0.32	0.68			
Q9UL40	Zinc finger protein 346	2	6	-0.52	-0.30	0.09			
P47974	Zinc finger protein 36, C3H1 type-like 2	3	8	-0.04	0.20	0.26			
Q8TF68	Zinc finger protein 384	4	18	-0.29	-0.07	0.08			
Q96B54	Zinc finger protein 428	3	11	0.09	0.15	0.12			
Q8N0Y2	Zinc finger protein 444	1	1	0.90	1.19	0.27			
Q9Y4E5	Zinc finger protein 451	1	1	0.07	0.06	0.00			
Q8NB15	Zinc finger protein 511	1	1	0.35	-0.57	-0.91			
Q96ME7	Zinc finger protein 512	10	37	0.19	-0.17	-0.41			
Q96KM6	Zinc finger protein 512B	7	13	-0.10	-0.33	-0.30			
Q6ZN55	Zinc finger protein 574	5	10	-0.30	0.06	0.26			
Q96N58	Zinc finger protein 578	1	1	0.01	0.20	0.20			
Q92610	Zinc finger protein 592	1	3	-0.38	-0.22	-0.01			
O00488	Zinc finger protein 593	1	1	0.06	-0.34	-0.40			
Q86UK7	Zinc finger protein 598	2	13	-0.19	-0.13	0.06			
O15014	Zinc finger protein 609	3	3	-0.06	-0.24	-0.12			
Q969S3	Zinc finger protein 622	4	4	-0.72	-0.52	0.20			
Q14966	Zinc finger protein 638	16	38	-0.11	-0.14	-0.02			
Q9Y2D9	Zinc finger protein 652	3	4	-0.01	-0.31	-0.30			
Q96K58	Zinc finger protein 668	1	1	-0.05	0.09	0.12			
Q8N1G0	Zinc finger protein 687	4	7	-0.24	-0.01	0.28			
P0C7X2	Zinc finger protein 688	1	1	-0.44	-0.15	0.29			
Q9H7X3	Zinc finger protein 696	1	1	-0.27	-0.48	-0.20			
Q9Y5V0	Zinc finger protein 706	1	2	0.01	-0.93	-0.95			
Q8NDX6	Zinc finger protein 740	1	2	0.09	-0.01	-0.10			
P36508	Zinc finger protein 76	1	9	-0.11	-0.08	0.02			
Q6DD87	Zinc finger protein 787	2	2	0.00	0.84	0.85			
P17098	Zinc finger protein 8	1	2	-0.14	-0.04	0.11			
Q2TB10	Zinc finger protein 800	4	6	-0.25	-0.21	-0.04			
Q96NB3	Zinc finger protein 830	1	6	-0.32	-0.15	0.17			
Q5JPB2	Zinc finger protein 831	1	1	-0.23	0.89	1.14			
P0CJ79	Zinc finger protein 888	1	2	NA	NA	NA			
Q9UKT9	Zinc finger protein Aiolos	5	27	-0.97	-0.84	0.14	5	5	
Q9UKS7	Zinc finger protein Helios	2	3	-0.13	0.31	0.44			
Q92785	Zinc finger protein ubi-d4	10	37	-0.13	-0.01	0.07			
P17029	Zinc finger protein with KRAB and SCAN domains 1	1	1	0.06	0.21	0.15			
Q8IX07	Zinc finger protein ZFPM1	2	2	-0.54	-0.16	0.38			
O75312	Zinc finger protein ZPR1	6	21	0.18	-0.07	-0.29			
Q2QGD7	Zinc finger protein ZXDC	1	1	-0.08	0.03	0.12			
O95218	Zinc finger Ran-binding domain-containing protein 2	7	15	-0.23	-0.43	0.11			
Q96KR1	Zinc finger RNA-binding protein	7	31	-0.02	0.01	-0.03			
A7E2V4	Zinc finger SWIM domain-containing protein 8	1	1	0.67	0.02	-0.64			
P08048	Zinc finger Y-chromosomal protein	1	1	-0.60	0.15	0.75			
O43149	Zinc finger ZZ-type and EF-hand domain-containing protein 1	9	17	-0.01	0.38	0.37			
Q9Y6X8	Zinc fingers and homeoboxes protein 2	7	12	-0.24	0.01	0.23			
Q9H4I2	Zinc fingers and homeoboxes protein 3	1	2	-0.79	-0.16	0.64			
Q9BQ52	Zinc phosphodiesterase ELAC protein 2	12	33	0.03	-0.20	-0.23			
Q6NXT4	Zinc transporter 6	1	1	NA	NA	NA			
Q6PML9	Zinc transporter 9	1	1	0.44	0.40	-0.02			
P25311	Zinc-alpha-2-glycoprotein	2	7	0.71	0.09	-0.15	3		
Q8N4Q0	Zinc-binding alcohol dehydrogenase domain-containing protein 2	4	7	0.45	0.32	-0.13			
Q15942	Zyxin	16	166	-0.30	-0.20	0.01			

List of Figures

1	The relation between the innate and the adaptive immune response	3
2	Components of the innate and adaptive immune system	3
3	NK cells adjust immune cell responses	6
4	Formation of the immunological synapse in NK cells	7
5	Stimulation and activation of CD8 ⁺ T cells	8
6	Formation of the immunological synapse	10
7	Surface markers and transcription factors of a typical, adult MAIT cell	12
8	Presentation of riboflavin metabolites activates MAIT cells	14
9	MAIT cell effector functions	15
10	Schematic view on MAIT cell development	16
11	Gating strategy to study effector functions of human CD3 ⁺ CD56 ⁺ NK cells . .	38
12	NK cell cytokine production is induced by K562 target cells	39
13	Inhibition of Src family kinases, CaMKII and PKD decreases NK cell degranulation and cytokine release in primary human PBMCs	40
14	Donor-specific responses of pure NK cells treated with Dasatinib, CK59 and CID755673	42
15	Gating strategy for primary human MAIT cells	44
16	Percentage of MAIT cells in various human donors	45
17	Activation of primary human MAITs with <i>E. coli</i>	46
18	Gating strategy for the isolation of primary human MAIT cells via FACS . . .	48
19	MS/MS spectrum of cytolytic perforin peptide ISALTALR	49
20	Localization of proteins identified in a proteomic analysis of MAIT cells	50
21	Chromatogram of SCX subfractionation of 250 000 cells	53
22	Localization of proteins identified in a proteomic analysis of primary human PBMCs	54
23	MS/MS spectrum of an iTRAQ-labeled peptide of actin	55
24	Differentially labeled samples from the same experiment show high reproducibility	56

25	Isolation of primary human MAIT, NK and CD8 ⁺ T cells from PBMC cultures	58
26	SCX subfractionation chromatogram shows presence of peptide in different fractions	61
27	Number of identified proteins in MAIT, NK and cCD8 ⁺ cells from five human donors	61
28	Pathway annotation of all identified proteins in MAIT, NK and cCD8 ⁺ cells . .	62
29	MS/MS spectrum of an iTRAQ-labeled peptide of marker protein CD8, alpha chain	64
30	Distribution of the regulation factors in five donors shows distinct differences between MAIT, NK and cCD8 ⁺ T cells	65
31	Heat maps of log ₂ regulation factors determined by iTRAQ-based LC-MS/MS from primary human MAIT, NK and cCD8 ⁺ T cells.	66
32	Expression of CD48 and CD98 on MAIT, NK and cCD8 ⁺ T cells	71
33	GeneGo enrichment analysis of MAIT proteins, compared to cCD8 ⁺ T cells. .	74
34	Formation of the MAIT immunological synapse	80
35	S100A4 forms structures with microtubules in MAIT cells	82
36	S100A4 recruitment towards microtubules and the immunological synapse upon activation	83
37	S100A4 localizes at the MAIT immunological synapse	85
38	Schematic representation of known and potential interactions between PKC and PKD family kinase isoforms	90
39	Similarity between human NK, MAIT and cCD8 ⁺ T cells	96
40	Differential abundance of effector molecules in cCD8 ⁺ T, MAIT and NK cells .	100
41	Proteomic definition of a typical primary human MAIT cell	105
42	A first view on MAIT cell IS formation and proliferation control	108

List of Tables

1	Small molecule kinase inhibitors	22
2	Used cell lines	22
3	Antibodies panel used for flow cytometry	23
4	Primary antibodies used for immunofluorescence	23
5	Secondary antibodies used for immunofluorescence	24
6	Used Mascot search parameters	32
7	Used filters in ProteomeDiscoverer	32
8	Selected proteins with immunological function identified in MAIT cells	50
9	Pilot study of the MAIT proteome indicates the presence of T cell specific pathways	51
10	Donor information, purity and cell number of sorted MAIT, NK and CD8 ⁺ T cells	59
11	Number of identified proteins per donor	60
12	Number of regulated proteins per compared cell types	68
13	List of proteins regulated in all five donors	69
14	Significantly regulated proof of concept-proteins in MAIT, NK and cCD8 ⁺ T cells	70
15	Regulation of effector molecules in MAIT, NK and cCD8 ⁺ T cells	73
16	Proteins strongly upregulated in MAIT:cCD8 ⁺ and associated with GeneGo molecular process “exocytosis”	75
17	Top twenty regulated proteins between MAIT cells and cCD8 ⁺ T cells	76
18	Proteins exclusively upregulated in MAIT cells	78

List of Abbreviations

5-A-RU	5-amino-6-D-ribitylaminouracil
ACN	acetonitrile
ADCC	antibody-dependent cellular cytotoxicity
ALL	acute lymphoblastic leukemia
APC	antigen-presenting cell
BCR	B cell receptor
BSA	bovine serum albumin
C	cysteine
CaMKII	Ca ²⁺ /calmodulin-dependent protein kinase II
cCD8 ⁺	conventionall CD8 ⁺ T cells
CD	cluster of differentiation
CDI	<i>Clostridium difficile</i> infection
CML	chronic myelogenous leukemia
Da	Dalton
DAPI	4',6-diamidino-2-phenylindole
DAVID	Database for Annotation, Visualization and Integrated Discovery
DC	dendritic cells
DCM	dead cell marker
DFF45	DNA Fragmentation Factor 45

DMSO	dimethyl sulfoxide
DN	double negative T cell (CD4 [−] CD8 [−])
E:T ratio	effector-to-target cell ratio
EDTA	ethylenediaminetetraacetic acid
FA	formic acid
FACS	fluorescence-activated cell sorting
FBS	fetal bovine serum
FSC	forward scatter
GO	gene ontology
GzmA	granzyme A
GzmB	granzyme B
GzmH	granzyme H
GzmK	granzyme K
GzmM	granzyme M
HCD	higher-energy collisional dissociation
IAP	inhibitor of apoptosis protein
ICAD	inhibitor of caspase-activated DNase
ICAM	intercellular adhesion molecule
ICOS	inducible costimulator
IF	immunofluorescence
IFN- γ	interferon- γ
IL18-R α	interleukin 18-receptor α
IL4I1	IL-4-induced gene 1
IS	immunological synapse

ITAM	immunoreceptor tyrosine-based activating motif
ITIM	immunoreceptor tyrosine based-inhibition motif
iTRAQ	isobaric tags for relative and absolute quantitation
K	lysine
LAAO	L-amino-acid oxidase
LAMP-1	Lysosome-associated membrane glycoprotein 1
LB medium	lysogeny broth medium
LC	liquid chromatography
LFA-1	Lymphocyte function-associated antigen-1
LGL	large granular lymphocyte
LPS	lipopolysaccharide
M	methionine
mAb	monoclonal antibody
MACS	magnetic activated cell sorting
MAD	median absolute deviation from the median
MAIT	mucosal-associated invariant T cell
MDR1	Multidrug resistance protein 1
MFI	median fluorescence intensity
MHC	major histocompatibility complex
MMTS	methyl methanethiosulfonate
MOI	multiplicity of infection
MS	mass spectrometry
MTOC	microtubule-organizing center
N-term	N-terminal

NK cell	natural killer cell
PBMC	peripheral blood mononuclear cell
PBS	phosphate buffered saline
PFA	paraformaldehyde
PKC	protein kinase C
PKD	protein kinase D
ppm	parts per million
RF	regulation factor
ROR γ t	Retinoic acid-related orphan receptor γ t
RT	room temperature
SCX chromatography	strong cation exchange chromatography
SMAC	supramolecular activation complex
SSC	sideward scatter
TCEP	tris(2-carboxyethyl)phosphine
TCR	T cell receptor
TCR-MC	TCR-microclusters
TEAB	tetraethylammonium bromide
TFA	trifluoroacetic acid
TNF- α	tumor necrosis factor- α
TNFR	tumor necrosis factor receptors
UV	ultra violet
w/w	weight per weight
WASP	Wiskott-Aldrich syndrome protein

Used abbreviations that are not in this list are in accordance with international standards as defined in the Instruction to Authors of the European Journal of Biochemistry.²⁶²

Bibliography

- [1] Murphy, K., Travers, P., Walport, M. & Janeway, C. *Janeway's Immunobiology* (Garland Science, New York, 2012).
- [2] Sun, J. C., Ugolini, S. & Vivier, E. Immunological memory within the innate immune system. *EMBO J* **33**, 1295–303 (2014).
- [3] Quintin, J., Cheng, S.-C., van der Meer, J. W. M. & Netea, M. G. Innate immune memory: towards a better understanding of host defense mechanisms. *Curr Opin Immunol* **29**, 1–7 (2014).
- [4] Godfrey, D. I., Stankovic, S. & Baxter, A. G. Raising the NKT cell family. *Nat Immunol* **11**, 197–206 (2010).
- [5] Gao, Y. & Williams, A. P. Role of Innate T Cells in Anti-Bacterial Immunity. *Front Immunol* **6**, 302 (2015).
- [6] Gapin, L. Where do MAIT cells fit in the family of unconventional T cells? *PLoS Biol* **7**, e70 (2009).
- [7] Gapin, L. Check MAIT. *J Immunol* **192**, 4475–80 (2014).
- [8] Margulies, D. H. The in-betweeners: MAIT cells join the innate-like lymphocytes gang. *J Exp Med* **211**, 1501–2 (2014).
- [9] Kumar, S. Cellular and Molecular Immunology. URL <http://nptel.ac.in/courses/102103038/>.
- [10] Dranoff, G. Cytokines in cancer pathogenesis and cancer therapy. *Nat Rev Cancer* **4**, 11–22 (2004).
- [11] Vivier, E., Tomasello, E., Baratin, M., Walzer, T. & Ugolini, S. Functions of natural killer cells. *Nat Immunol* **9**, 503–510 (2008).
- [12] Caligiuri, M. A. Human natural killer cells. *Blood* **112**, 461–9 (2008).

- [13] Bryceson, Y. T., Ljunggren, H.-G. & Long, E. O. Minimal requirement for induction of natural cytotoxicity and intersection of activation signals by inhibitory receptors. *Blood* **114**, 2657–66 (2009).
- [14] Fauriat, C., Long, E. O., Ljunggren, H.-G. & Bryceson, Y. T. Regulation of human NK-cell cytokine and chemokine production by target cell recognition. *Blood* **115**, 2167–2176 (2010).
- [15] Alter, G., Malenfant, J. M. & Altfeld, M. CD107a as a functional marker for the identification of natural killer cell activity. *J Immunol Methods* **294**, 15–22 (2004).
- [16] Cooper, M. A. *et al.* Human natural killer cells: a unique innate immunoregulatory role for the CD56(bright) subset. *Blood* **97**, 3146–51 (2001).
- [17] Cooper, M. A., Fehniger, T. A. & Caligiuri, M. A. The biology of human natural killer-cell subsets. *Trends Immunol* **22**, 633–640 (2001).
- [18] Moretta, L. Dissecting CD56dim human NK cells. *Blood* **116**, 3689–91 (2010).
- [19] Scheiter, M. *et al.* Proteome analysis of distinct developmental stages of human natural killer (NK) cells. *Mol Cell Proteomics* **12**, 1099–114 (2013).
- [20] Björkström, N. K., Ljunggren, H.-G. & Sandberg, J. K. CD56 negative NK cells: origin, function, and role in chronic viral disease. *Trends Immunol* **31**, 401–6 (2010).
- [21] Vivier, E., Nunès, J. A. & Vély, F. Natural killer cell signaling pathways. *Science (80-)* **306**, 1517–1519 (2004).
- [22] Lanier, L. L. NK cell recognition. *Annu Rev Immunol* **23**, 225–74 (2005).
- [23] Bryceson, Y. T., March, M. E., Ljunggren, H.-G. & Long, E. O. Activation, coactivation, and costimulation of resting human natural killer cells. *Immunol Rev* **214**, 73–91 (2006).
- [24] Bryceson, Y. T., March, M. E., Ljunggren, H.-G. & Long, E. O. Activation, coactivation, and costimulation of resting human natural killer cells. *Immunol Rev* **214**, 73–91 (2006).
- [25] Lanier, L. L. Up on the tightrope: natural killer cell activation and inhibition. *Nat Immunol* **9**, 495–502 (2008).
- [26] Bryceson, Y. T. *et al.* Molecular Mechanisms of Natural Killer Cell Activation. *J Innate Immun* **3**, 216–226 (2011).

-
- [27] Krzewski, K. & Coligan, J. E. Human NK cell lytic granules and regulation of their exocytosis. *Front Immunol* **3**, 335 (2012).
- [28] Forthal, D. N. *et al.* Antibody-dependent cellular cytotoxicity independently predicts survival in severely immunocompromised human immunodeficiency virus-infected patients. *J Infect Dis* **180**, 1338–41 (1999).
- [29] Kärre, K., Ljunggren, H. G., Piontek, G. & Kiessling, R. Selective rejection of H-2-deficient lymphoma variants suggests alternative immune defence strategy. *Nature* **319**, 675–8 (1986).
- [30] Hanson, M. G. V. *et al.* A short-term dietary supplementation with high doses of vitamin E increases NK cell cytolytic activity in advanced colorectal cancer patients. *Cancer Immunol Immunother* **56**, 973–84 (2007).
- [31] Li, C. *et al.* JNK MAP kinase activation is required for MTOC and granule polarization in NKG2D-mediated NK cell cytotoxicity. *Proc Natl Acad Sci U S A* **105**, 3017–22 (2008).
- [32] Brandt, C. S. *et al.* The B7 family member B7-H6 is a tumor cell ligand for the activating natural killer cell receptor NKp30 in humans. *J Exp Med* **206**, 1495–503 (2009).
- [33] Moretta, A., Biassoni, R., Bottino, C., Mingari, M. C. & Moretta, L. Natural cytotoxicity receptors that trigger human NK-cell-mediated cytotoxicity. *Immunol Today* **21**, 228–34 (2000).
- [34] Lanier, L. L., Yu, G. & Phillips, J. H. Co-association of CD3 zeta with a receptor (CD16) for IgG Fc on human natural killer cells. *Nature* **342**, 803–5 (1989).
- [35] Wirthmueller, U., Kurosaki, T., Murakami, M. S. & Ravetch, J. V. Signal transduction by Fc gamma RIII (CD16) is mediated through the gamma chain. *J Exp Med* **175**, 1381–90 (1992).
- [36] Kumar, V. & McEnerney, M. E. A new self: MHC-class-I-independent natural-killer-cell self-tolerance. *Nat Rev Immunol* **5**, 363–74 (2005).
- [37] Riteau, B., Barber, D. F. & Long, E. O. Vav1 phosphorylation is induced by beta2 integrin engagement on natural killer cells upstream of actin cytoskeleton and lipid raft reorganization. *J Exp Med* **198**, 469–74 (2003).

- [38] Perez, O. D., Mitchell, D., Jager, G. C. & Nolan, G. P. LFA-1 signaling through p44/42 is coupled to perforin degranulation in CD56+CD8+ natural killer cells. *Blood* **104**, 1083–93 (2004).
- [39] Chen, X. *et al.* CD28-stimulated ERK2 phosphorylation is required for polarization of the microtubule organizing center and granules in YTS NK cells. *Proc Natl Acad Sci U S A* **103**, 10346–51 (2006).
- [40] Orange, J. S. *et al.* The mature activating natural killer cell immunologic synapse is formed in distinct stages. *Proc Natl Acad Sci U S A* **100**, 14151–6 (2003).
- [41] Bryceson, Y. T., March, M. E., Barber, D. F., Ljunggren, H.-G. & Long, E. O. Cytolytic granule polarization and degranulation controlled by different receptors in resting NK cells. *J Exp Med* **202**, 1001–12 (2005).
- [42] Orange, J. S. Formation and function of the lytic NK-cell immunological synapse. *Nat Rev Immunol* **8**, 713–25 (2008).
- [43] König, S. *et al.* Kinome Analysis of Receptor-Induced Phosphorylation in Human Natural Killer Cells (2012).
- [44] Dustin, M. L. & Springer, T. A. T-cell receptor cross-linking transiently stimulates adhesiveness through LFA-1. *Nature* **341**, 619–624 (1989).
- [45] Dustin, M. L. Coordination of T cell activation and migration through formation of the immunological synapse. *Ann N Y Acad Sci* **987**, 51–9 (2003).
- [46] Scholer, A., Hugues, S., Boissonnas, A., Fetler, L. & Amigorena, S. Intercellular Adhesion Molecule-1-Dependent Stable Interactions between T Cells and Dendritic Cells Determine CD8+ T Cell Memory. *Immunity* **28**, 258–270 (2008).
- [47] Wang, S. *et al.* Costimulation of T cells by B7-H2, a B7-like molecule that binds ICOS. *Blood* **96**, 2808–13 (2000).
- [48] Gonzalo, J. A. *et al.* Cutting edge: the related molecules CD28 and inducible costimulator deliver both unique and complementary signals required for optimal T cell activation. *J Immunol* **166**, 1–5 (2001).
- [49] Bour-Jordan, H. & Blueston, J. A. CD28 function: a balance of costimulatory and regulatory signals. *J Clin Immunol* **22**, 1–7 (2002).

-
- [50] Zhou, X.-Y. *et al.* Molecular mechanisms underlying differential contribution of CD28 versus non-CD28 costimulatory molecules to IL-2 promoter activation. *J Immunol* **168**, 3847–54 (2002).
- [51] Watts, T. H. TNF/TNFR family members in costimulation of T cell responses. *Annu Rev Immunol* **23**, 23–68 (2005).
- [52] Greenwald, R. J., Freeman, G. J. & Sharpe, A. H. The B7 family revisited. *Annu Rev Immunol* **23**, 515–48 (2005).
- [53] Croft, M. Activation of naive, memory and effector T cells. *Curr Opin Immunol* **6**, 431–7 (1994).
- [54] Shimizu, Y., Van Seventer, G. A., Horgan, K. J. & Shaw, S. Regulated expression and binding of three VLA (beta 1) integrin receptors on T cells. *Nature* **345**, 250–3 (1990).
- [55] Hviid, L., Odum, N. & Theander, T. G. The relation between T-cell expression of LFA-1 and immunological memory. *Immunology* **78**, 237–43 (1993).
- [56] Hamann, D. *et al.* Phenotypic and functional separation of memory and effector human CD8+ T cells. *J Exp Med* **186**, 1407–18 (1997).
- [57] Dustin, M. L. & Long, E. O. Cytotoxic immunological synapses. *Immunol Rev* **235**, 24–34 (2010).
- [58] Le Floch, A. & Huse, M. Molecular mechanisms and functional implications of polarized actin remodeling at the T cell immunological synapse. *Cell Mol Life Sci* **72**, 537–56 (2015).
- [59] Yasukawa, M. *et al.* Granule exocytosis, and not the fas/fas ligand system, is the main pathway of cytotoxicity mediated by alloantigen-specific CD4(+) as well as CD8(+) cytotoxic T lymphocytes in humans. *Blood* **95**, 2352–5 (2000).
- [60] Bossi, G. *et al.* The secretory synapse: the secrets of a serial killer. *Immunol Rev* **189**, 152–60 (2002).
- [61] Montoya, M. C., Sancho, D., Vicente-Manzanares, M. & Sánchez-Madrid, F. Cell adhesion and polarity during immune interactions. *Immunol Rev* **186**, 68–82 (2002).
- [62] Trambas, C. M. & Griffiths, G. M. Delivering the kiss of death. *Nat Immunol* **4**, 399–403 (2003).

- [63] Voskoboinik, I., Smyth, M. J. & Trapani, J. A. Perforin-mediated target-cell death and immune homeostasis. *Nat Rev Immunol* **6**, 940–52 (2006).
- [64] Ewen, C. L., Kane, K. P. & Bleackley, R. C. A quarter century of granzymes. *Cell Death Differ* **19**, 28–35 (2012).
- [65] Clayberger, C. & Krensky, A. M. Granulysin. *Curr Opin Immunol* **15**, 560–5 (2003).
- [66] Harty, J. T., Tvinnereim, A. R. & White, D. W. CD8+ T Cell Effector Mechanisms in Resistance to Infection. *Annu Rev Immunol* **18**, 275–308 (2000).
- [67] Harty, J. T. & Bevan, M. J. Responses of CD8(+) T cells to intracellular bacteria. *Curr Opin Immunol* **11**, 89–93 (1999).
- [68] Andersen, M. H., Schrama, D., Thor Straten, P. & Becker, J. C. Cytotoxic T cells. *J Invest Dermatol* **126**, 32–41 (2006).
- [69] Hehlhans, T. & Männel, D. N. The TNF-TNF receptor system. *Biol Chem* **383**, 1581–5 (2002).
- [70] Liuzzi, A. R., McLaren, J. E., Price, D. A. & Eberl, M. Early innate responses to pathogens: pattern recognition by unconventional human T-cells. *Curr Opin Immunol* **36**, 31–37 (2015).
- [71] Rossjohn, J., Pellicci, D. G., Patel, O., Gapin, L. & Godfrey, D. I. Recognition of CD1d-restricted antigens by natural killer T cells. *Nat Rev Immunol* **12**, 845–57 (2012).
- [72] Bendelac, A., Savage, P. B. & Teyton, L. The biology of NKT cells. *Annu Rev Immunol* **25**, 297–336 (2007).
- [73] Tilloy, F. *et al.* An invariant T cell receptor alpha chain defines a novel TAP-independent major histocompatibility complex class Ib-restricted alpha/beta T cell subpopulation in mammals. *J Exp Med* **189**, 1907–21 (1999).
- [74] Griewank, K. *et al.* Homotypic interactions mediated by Slamf1 and Slamf6 receptors control NKT cell lineage development. *Immunity* **27**, 751–62 (2007).
- [75] Shimamura, M. *et al.* Localization of NK1.1(+) invariant Valpha19 TCR(+) cells in the liver with potential to promptly respond to TCR stimulation. *Immunol Lett* **121**, 38–44 (2008).
- [76] Martin, E. *et al.* Stepwise development of MAIT cells in mouse and human. *PLoS Biol* **7**, e54 (2009).

-
- [77] Billerbeck, E. *et al.* Analysis of CD161 expression on human CD8+ T cells defines a distinct functional subset with tissue-homing properties. *Proc Natl Acad Sci U S A* **107**, 3006–11 (2010).
- [78] Ussher, J. E., Klenerman, P. & Willberg, C. B. Mucosal-associated invariant T-cells: new players in anti-bacterial immunity. *Front Immunol* **5**, 450 (2014).
- [79] Le Bourhis, L. *et al.* Antimicrobial activity of mucosal-associated invariant T cells. *Nat Immunol* **11**, 701–8 (2010).
- [80] Dusseaux, M. *et al.* Human MAIT cells are xenobiotic-resistant, tissue-targeted, CD161hi IL-17-secreting T cells. *Blood* **117**, 1250–9 (2011).
- [81] Treiner, E. *et al.* Selection of evolutionarily conserved mucosal-associated invariant T cells by MR1. *Nature* **422**, 164–9 (2003).
- [82] Sharma, P. K. *et al.* High Expression of CD26 Accurately Identifies Human Bacterial-Reactive MR1-restricted MAIT cells. *Immunology* (2015).
- [83] Fox, D. A. *et al.* Ta1, a novel 105 KD human T cell activation antigen defined by a monoclonal antibody. *J Immunol* **133**, 1250–6 (1984).
- [84] Fleischer, B. A novel pathway of human T cell activation via a 103 kD T cell activation antigen. *J Immunol* **138**, 1346–50 (1987).
- [85] Turtle, C. J., Swanson, H. M., Fujii, N., Estey, E. H. & Riddell, S. R. A distinct subset of self-renewing human memory CD8+ T cells survives cytotoxic chemotherapy. *Immunity* **31**, 834–44 (2009).
- [86] Johnstone, R. W., Ruefli, A. A. & Smyth, M. J. Multiple physiological functions for multidrug transporter P-glycoprotein? *Trends Biochem Sci* **25**, 1–6 (2000).
- [87] Mizutani, T. *et al.* Genuine functions of P-glycoprotein (ABCB1). *Curr Drug Metab* **9**, 167–74 (2008).
- [88] Geissmann, F. *et al.* Intravascular immune surveillance by CXCR6+ NKT cells patrolling liver sinusoids. *PLoS Biol* **3**, e113 (2005).
- [89] Sato, T. *et al.* Role for CXCR6 in recruitment of activated CD8+ lymphocytes to inflamed liver. *J Immunol* **174**, 277–83 (2005).
- [90] Maggi, L. *et al.* CD161 is a marker of all human IL-17-producing T-cell subsets and is induced by RORC. *Eur J Immunol* **40**, 2174–81 (2010).

- [91] Carlyle, J. R. *et al.* Missing self-recognition of Ocil/Clr-b by inhibitory NKR-P1 natural killer cell receptors. *Proc Natl Acad Sci U S A* **101**, 3527–32 (2004).
- [92] Rosen, D. B. *et al.* Cutting edge: lectin-like transcript-1 is a ligand for the inhibitory human NKR-P1A receptor. *J Immunol* **175**, 7796–9 (2005).
- [93] Aldemir, H. *et al.* Cutting edge: lectin-like transcript 1 is a ligand for the CD161 receptor. *J Immunol* **175**, 7791–5 (2005).
- [94] Le Bourhis, L. *et al.* MAIT Cells Detect and Efficiently Lyse Bacterially-Infected Epithelial Cells. *PLoS Pathog* **9**, e1003681 (2013).
- [95] Walker, L. J. *et al.* Human MAIT and CD8 $\alpha\alpha$ cells develop from a pool of type-17 precommitted CD8+ T cells. *Blood* **119**, 422–33 (2012).
- [96] Kreslavsky, T. *et al.* TCR-inducible PLZF transcription factor required for innate phenotype of a subset of gammadelta T cells with restricted TCR diversity. *Proc Natl Acad Sci U S A* **106**, 12453–8 (2009).
- [97] Savage, A. K. *et al.* The transcription factor PLZF directs the effector program of the NKT cell lineage. *Immunity* **29**, 391–403 (2008).
- [98] Le Bourhis, L. *et al.* Mucosal-associated invariant T cells: unconventional development and function. *Trends Immunol* **32**, 212–8 (2011).
- [99] Cosmi, L. *et al.* Human interleukin 17-producing cells originate from a CD161+CD4+ T cell precursor. *J Exp Med* **205**, 1903–16 (2008).
- [100] Le Bourhis, L., Mburu, Y. K. & Lantz, O. MAIT cells, surveyors of a new class of antigen: development and functions. *Curr Opin Immunol* **25**, 174–80 (2013).
- [101] Gold, M. C. *et al.* Human mucosal associated invariant T cells detect bacterially infected cells. *PLoS Biol* **8**, e1000407 (2010).
- [102] Riegert, P, Wanner, V & Bahram, S. Genomics, isoforms, expression, and phylogeny of the MHC class I-related MR1 gene. *J Immunol* **161**, 4066–77 (1998).
- [103] Huang, S. *et al.* MR1 antigen presentation to mucosal-associated invariant T cells was highly conserved in evolution. *Proc Natl Acad Sci U S A* **106**, 8290–5 (2009).
- [104] Young, M. H. *et al.* MAIT cell recognition of MR1 on bacterially infected and uninfected cells. *PLoS One* **8**, e53789 (2013).

-
- [105] Kjer-Nielsen, L. *et al.* MR1 presents microbial vitamin B metabolites to MAIT cells. *Nature* **491**, 717–23 (2012).
- [106] Corbett, A. J. *et al.* T-cell activation by transitory neo-antigens derived from distinct microbial pathways. *Nature* **509**, 361–5 (2014).
- [107] Eckle, S. B. G. *et al.* A molecular basis underpinning the T cell receptor heterogeneity of mucosal-associated invariant T cells. *J Exp Med* (2014).
- [108] Turtle, C. J. *et al.* Innate signals overcome acquired TCR signaling pathway regulation and govern the fate of human CD161(hi) CD8 α + semi-invariant T cells. *Blood* **118**, 2752–62 (2011).
- [109] Otani, T. *et al.* Identification of IFN-gamma-producing cells in IL-12/IL-18-treated mice. *Cell Immunol* **198**, 111–9 (1999).
- [110] Ussher, J. E. *et al.* CD161(++) CD8(+) T cells, including the MAIT cell subset, are specifically activated by IL-12+IL-18 in a TCR-independent manner. *Eur J Immunol* (2013).
- [111] Jo, J. *et al.* Toll-Like Receptor 8 Agonist and Bacteria Trigger Potent Activation of Innate Immune Cells in Human Liver. *PLoS Pathog* **10**, e1004210 (2014).
- [112] Illés, Z., Shimamura, M., Newcombe, J., Oka, N. & Yamamura, T. Accumulation of Valpha7.2-Jalpha33 invariant T cells in human autoimmune inflammatory lesions in the nervous system. *Int Immunol* **16**, 223–30 (2004).
- [113] Croxford, J. L., Miyake, S., Huang, Y.-Y., Shimamura, M. & Yamamura, T. Invariant V(alpha)19i T cells regulate autoimmune inflammation. *Nat Immunol* **7**, 987–94 (2006).
- [114] Miyazaki, Y., Miyake, S., Chiba, A., Lantz, O. & Yamamura, T. Mucosal-associated invariant T cells regulate Th1 response in multiple sclerosis. *Int Immunol* **23**, 529–35 (2011).
- [115] Teunissen, M. B. M. *et al.* The IL-17A-producing CD8+ T-cell population in psoriatic lesional skin comprises mucosa-associated invariant T cells and conventional T cells. *J Invest Dermatol* **134**, 2898–907 (2014).
- [116] Serriari, N.-E. *et al.* Innate Mucosal-Associated Invariant T (MAIT) cells are activated in Inflammatory Bowel Diseases. *Clin Exp Immunol* (2014).

- [117] Kurioka, A. *et al.* MAIT cells are licensed through granzyme exchange to kill bacterially sensitized targets. *Mucosal Immunol* (2014).
- [118] Gold, M. C. *et al.* Human thymic MR1-restricted MAIT cells are innate pathogen-reactive effectors that adapt following thymic egress. *Mucosal Immunol* **6**, 35–44 (2013).
- [119] McWilliam, H. E. G., Birkinshaw, R. W., Villadangos, J. A., McCluskey, J. & Rossjohn, J. MR1 presentation of vitamin B-based metabolite ligands. *Curr Opin Immunol* **34**, 28–34 (2015).
- [120] Leeansyah, E., Loh, L., Nixon, D. F. & Sandberg, J. K. Acquisition of innate-like microbial reactivity in mucosal tissues during human fetal MAIT-cell development. *Nat Commun* **5**, 3143 (2014).
- [121] Seach, N. *et al.* Double-positive thymocytes select mucosal-associated invariant T cells. *J Immunol* **191**, 6002–9 (2013).
- [122] Meierovics, A., Yankelevich, W.-J. C. & Cowley, S. C. MAIT cells are critical for optimal mucosal immune responses during in vivo pulmonary bacterial infection. *Proc Natl Acad Sci U S A* **110**, E3119–28 (2013).
- [123] Georgel, P., Radosavljevic, M., Macquin, C. & Bahram, S. The non-conventional MHC class I MR1 molecule controls infection by *Klebsiella pneumoniae* in mice. *Mol Immunol* **48**, 769–75 (2011).
- [124] Chua, W.-J. *et al.* Polyclonal mucosa-associated invariant T cells have unique innate functions in bacterial infection. *Infect Immun* **80**, 3256–67 (2012).
- [125] Wong, E. B. *et al.* Low Levels of Peripheral CD161++CD8+ Mucosal Associated Invariant T (MAIT) Cells Are Found in HIV and HIV/TB Co-Infection. *PLoS One* **8**, e83474 (2013).
- [126] Lee, O.-J. *et al.* Circulating mucosal-associated invariant T cell levels and their cytokine levels in healthy adults. *Exp Gerontol* **49**, 47–54 (2014).
- [127] Grimaldi, D. *et al.* Specific MAIT cell behaviour among innate-like T lymphocytes in critically ill patients with severe infections. *Intensive Care Med* (2013).
- [128] Leeansyah, E. *et al.* Activation, exhaustion, and persistent decline of the antimicrobial MR1-restricted MAIT-cell population in chronic HIV-1 infection. *Blood* **121**, 1124–35 (2013).

-
- [129] Cosgrove, C. *et al.* Early and nonreversible decrease of CD161⁺⁺ /MAIT cells in HIV infection. *Blood* **121**, 951–61 (2013).
- [130] Annibaldi, V. *et al.* CD161(high)CD8⁺T cells bear pathogenetic potential in multiple sclerosis. *Brain* **134**, 542–54 (2011).
- [131] Chiba, A. *et al.* Mucosal-associated invariant T cells promote inflammation and exacerbate disease in murine models of arthritis. *Arthritis Rheum* **64**, 153–61 (2012).
- [132] Peterfalvi, A. *et al.* Invariant Valpha7.2-Jalpha33 TCR is expressed in human kidney and brain tumors indicating infiltration by mucosal-associated invariant T (MAIT) cells. *Int Immunol* **20**, 1517–25 (2008).
- [133] Klawonn, F. Significance tests to identify regulated proteins based on a large number of small samples. *Kybernetika* **48**, 478–493 (2012).
- [134] König, S. *et al.* Kinome analysis of receptor-induced phosphorylation in human natural killer cells. *PLoS One* **7**, e29672 (2012).
- [135] Scheiter, M. *et al.* Protein kinase inhibitors CK59 and CID755673 alter primary human NK cell effector functions. *Front Immunol* **4** (2013).
- [136] Bryceson, Y. T. *et al.* Functional Analysis of Human NK Cells by Flow Cytometry. In Campbell, K. S. (ed.) *Nat Kill Cell Protoc*, vol. 612 of *Methods in Molecular Biology*, 335–352 (Humana Press, 2010).
- [137] Novak, J., Dobrovolny, J., Novakova, L. & Kozak, T. The decrease in number and change in phenotype of mucosal-associated invariant T cells in the elderly and differences in males and females of reproductive age. *Scand J Immunol* (2014).
- [138] Walker, L. J., Klenerman, P. & Tharmalingam, H. The rise and fall of MAIT cells with age. *Scand J Immunol* (2014).
- [139] Fagerberg, L. *et al.* Mapping the subcellular protein distribution in three human cell lines. *J Proteome Res* **10**, 3766–77 (2011).
- [140] Huang, D. W., Sherman, B. T. & Lempicki, R. A. Systematic and integrative analysis of large gene lists using DAVID bioinformatics resources. *Nat Protoc* **4**, 44–57 (2009).
- [141] Huang, D. W., Sherman, B. T. & Lempicki, R. A. Bioinformatics enrichment tools: paths toward the comprehensive functional analysis of large gene lists. *Nucleic Acids Res* **37**, 1–13 (2009).

- [142] Hughes, C. S. *et al.* Ultrasensitive proteome analysis using paramagnetic bead technology. *Mol Syst Biol* **10**, 757 (2014).
- [143] Ross, P. L. *et al.* Multiplexed protein quantitation in *Saccharomyces cerevisiae* using amine-reactive isobaric tagging reagents. *Mol Cell Proteomics* **3**, 1154–69 (2004).
- [144] Morice, W. G. The immunophenotypic attributes of NK cells and NK-cell lineage lymphoproliferative disorders. *Am J Clin Pathol* **127**, 881–6 (2007).
- [145] Jacobs, R. *et al.* CD56bright cells differ in their KIR repertoire and cytotoxic features from CD56dim NK cells. *Eur J Immunol* **31**, 3121–7 (2001).
- [146] Fergusson, J. R. *et al.* CD161 Defines a Transcriptional and Functional Phenotype across Distinct Human T Cell Lineages. *Cell Rep* **9**, 1075–1088 (2014).
- [147] Way, G., Morrice, N., Smythe, C. & O’Sullivan, A. J. Purification and identification of secernin, a novel cytosolic protein that regulates exocytosis in mast cells. *Mol Biol Cell* **13**, 3344–54 (2002).
- [148] Sjöblom, B., Salmazo, A. & Djinoić-Carugo, K. Alpha-actinin structure and regulation. *Cell Mol Life Sci* **65**, 2688–701 (2008).
- [149] Willshaw, A. *et al.* Identification of a novel protein complex containing annexin A4, rabphilin and synaptotagmin. *FEBS Lett* **559**, 13–21 (2004).
- [150] Cordonnier, M. N., Dauzonne, D., Louvard, D. & Coudrier, E. Actin filaments and myosin I alpha cooperate with microtubules for the movement of lysosomes. *Mol Biol Cell* **12**, 4013–29 (2001).
- [151] Holt, O. *et al.* Slp1 and Slp2-a localize to the plasma membrane of CTL and contribute to secretion from the immunological synapse. *Traffic* **9**, 446–57 (2008).
- [152] Kapuscinski, J. DAPI: a DNA-specific fluorescent probe. *Biotech Histochem* **70**, 220–33 (1995).
- [153] Praper, T. *et al.* Human perforin employs different avenues to damage membranes. *J Biol Chem* **286**, 2946–55 (2011).
- [154] Krieg, S. & Ullrich, E. Novel immune modulators used in hematology: impact on NK cells. *Front Immunol* **3**, 388 (2012).

-
- [155] Lombardo, L. J. *et al.* Discovery of N-(2-chloro-6-methyl- phenyl)-2-(6-(4-(2-hydroxyethyl)- piperazin-1-yl)-2-methylpyrimidin-4- ylamino)thiazole-5-carboxamide (BMS-354825), a dual Src/Abl kinase inhibitor with potent antitumor activity in preclinical assays. *J Med Chem* **47**, 6658–6661 (2004).
- [156] Blake, S. J., Bruce Lyons, A., Fraser, C. K., Hayball, J. D. & Hughes, T. P. Dasatinib suppresses in vitro natural killer cell cytotoxicity. *Blood* **111**, 4415–4416 (2008).
- [157] Fraser, C. K. *et al.* Dasatinib inhibits recombinant viral antigen-specific murine CD4+ and CD8+ T-cell responses and NK-cell cytolytic activity in vitro and in vivo. *Exp Hematol* **37**, 256–265 (2009).
- [158] Salih, J. *et al.* The BCR/ABL-inhibitors imatinib, nilotinib and dasatinib differentially affect NK cell reactivity. *Int J Cancer* **127**, 2119–2128 (2010).
- [159] Hassold, N. *et al.* Enhancement of natural killer cell effector functions against selected lymphoma and leukemia cell lines by dasatinib. *Int J Cancer* **131**, E916—E927 (2012).
- [160] Konstantopoulos, N. *et al.* A purine analog kinase inhibitor, calcium/calmodulin-dependent protein kinase II inhibitor 59, reveals a role for calcium/calmodulin-dependent protein kinase II in insulin-stimulated glucose transport. *Endocrinology* **148**, 374–385 (2007).
- [161] Poggi, A. *et al.* NK cell activation by dendritic cells is dependent on LFA-1-mediated induction of calcium-calmodulin kinase II: inhibition by HIV-1 Tat C-terminal domain. *J Immunol* **168**, 95–101 (2002).
- [162] Sharlow, E. R. *et al.* Potent and selective disruption of protein kinase D functionality by a benzoxoloazepinolone. *J Biol Chem* **283**, 33516–33526 (2008).
- [163] Sturany, S. *et al.* Molecular cloning and characterization of the human protein kinase D2. A novel member of the protein kinase D family of serine threonine kinases. *J Biol Chem* **276**, 3310–3318 (2001).
- [164] Matthews, S. A. *et al.* Protein kinase D isoforms are dispensable for integrin-mediated lymphocyte adhesion and homing to lymphoid tissues. *Eur J Immunol* **42**, 1316–1326 (2012).
- [165] Larsson, M. & Broman, J. Different basal levels of CaMKII phosphorylated at Thr286/287 at nociceptive and low-threshold primary afferent synapses. *Eur J Neurosci* **21**, 2445–58 (2005).

- [166] Yuan, J., Bae, D., Cantrell, D., Nel, A. E. & Rozengurt, E. Protein kinase D is a downstream target of protein kinase C θ . *Biochem Biophys Res Commun* **291**, 444–52 (2002).
- [167] Rozengurt, E., Rey, O. & Waldron, R. T. Protein kinase D signaling. *J Biol Chem* **280**, 13205–13208 (2005).
- [168] Döppler, H. & Storz, P. A novel tyrosine phosphorylation site in protein kinase D contributes to oxidative stress-mediated activation. *J Biol Chem* **282**, 31873–31881 (2007).
- [169] Waldron, R. T., Iglesias, T. & Rozengurt, E. The pleckstrin homology domain of protein kinase D interacts preferentially with the η isoform of protein kinase C. *J Biol Chem* **274**, 9224–30 (1999).
- [170] Brändlin, I., Eiseler, T., Salowsky, R. & Johannes, F.-J. Protein kinase C μ regulation of the JNK pathway is triggered via phosphoinositide-dependent kinase 1 and protein kinase C ϵ . *J Biol Chem* **277**, 45451–7 (2002).
- [171] Tassi, I. *et al.* NK cell-activating receptors require PKC- θ for sustained signaling, transcriptional activation, and IFN- γ secretion. *Blood* **112**, 4109–4116 (2008).
- [172] Page, K. M., Chaudhary, D., Goldman, S. J. & Kasaian, M. T. Natural killer cells from protein kinase C θ -/- mice stimulated with interleukin-12 are deficient in production of interferon- γ . *J Leukoc Biol* **83**, 1267–1276 (2008).
- [173] Aguiló, J. I., Garaude, J., Pardo, J., Villalba, M. & Anel, A. Protein kinase C- θ is required for NK cell activation and in vivo control of tumor progression. *J Immunol* **182**, 1972–81 (2009).
- [174] Zhang, J., Yang, P. L. & Gray, N. S. Targeting cancer with small molecule kinase inhibitors. *Nat Rev Cancer* **9**, 28–39 (2009).
- [175] Talpaz, M. *et al.* Dasatinib in imatinib-resistant Philadelphia chromosome-positive leukemias. *N Engl J Med* **354**, 2531–41 (2006).
- [176] Lavalley, C. R. *et al.* Novel protein kinase D inhibitors cause potent arrest in prostate cancer cell growth and motility. *BMC Chem Biol* **10**, 5 (2010).
- [177] Schade, A. E. *et al.* Dasatinib, a small-molecule protein tyrosine kinase inhibitor, inhibits T-cell activation and proliferation. *Blood* **111**, 1366–1377 (2008).

-
- [178] Johansson, S., Berg, L., Hall, H. & Höglund, P. NK cells: elusive players in autoimmunity. *Trends Immunol* **26**, 613–8 (2005).
- [179] Schleinitz, N., Vély, F., Harlé, J.-R. & Vivier, E. Natural killer cells in human autoimmune diseases. *Immunology* **131**, 451–8 (2010).
- [180] Bareau, B. *et al.* Analysis of a French cohort of patients with large granular lymphocyte leukemia: a report on 229 cases. *Haematologica* **95**, 1534–41 (2010).
- [181] Watters, R. J., Liu, X. & Loughran, T. P. T-cell and natural killer-cell large granular lymphocyte leukemia neoplasias. *Leuk Lymphoma* **52**, 2217–25 (2011).
- [182] Suzuki, R. NK/T-cell lymphomas: pathobiology, prognosis and treatment paradigm. *Curr Oncol Rep* **14**, 395–402 (2012).
- [183] Wieczorek, L. *et al.* Mitigation of variation observed in a peripheral blood mononuclear cell (PBMC) based HIV-1 neutralization assay by donor cell pooling. *Virology* **447**, 240–8 (2013).
- [184] Maes, E., Landuyt, B., Mertens, I. & Schoofs, L. Interindividual variation in the proteome of human peripheral blood mononuclear cells. *PLoS One* **8**, e61933 (2013).
- [185] Boado, R. J., Li, J. Y., Nagaya, M., Zhang, C. & Pardridge, W. M. Selective expression of the large neutral amino acid transporter at the blood-brain barrier. *Proc Natl Acad Sci U S A* **96**, 12079–84 (1999).
- [186] Elishmereni, M. & Levi-Schaffer, F. CD48: A co-stimulatory receptor of immunity. *Int J Biochem Cell Biol* **43**, 25–8 (2011).
- [187] Sutton, V. R. & Trapani, J. A. Proteases in lymphocyte killer function: redundancy, polymorphism and questions remaining. *Biol Chem* **391**, 873–9 (2010).
- [188] Wensink, A. C., Hack, C. E. & Bovenschen, N. Granzymes Regulate Proinflammatory Cytokine Responses. *J Immunol* **194**, 491–497 (2015).
- [189] Voskoboinik, I., Whisstock, J. C. & Trapani, J. A. Perforin and granzymes: function, dysfunction and human pathology. *Nat Rev Immunol* (2015).
- [190] Martinvalet, D., Dykxhoorn, D. M., Ferrini, R. & Lieberman, J. Granzyme A cleaves a mitochondrial complex I protein to initiate caspase-independent cell death. *Cell* **133**, 681–92 (2008).

- [191] Martinvalet, D., Zhu, P & Lieberman, J. Granzyme A induces caspase-independent mitochondrial damage, a required first step for apoptosis. *Immunity* **22**, 355–70 (2005).
- [192] Chowdhury, D. *et al.* The exonuclease TREX1 is in the SET complex and acts in concert with NM23-H1 to degrade DNA during granzyme A-mediated cell death. *Mol Cell* **23**, 133–42 (2006).
- [193] Kaiserman, D. *et al.* Identification of Serpinb6b as a species-specific mouse granzyme A inhibitor suggests functional divergence between human and mouse granzyme A. *J Biol Chem* **289**, 9408–17 (2014).
- [194] Sower, L. E. *et al.* Extracellular activities of human granzyme A. Monocyte activation by granzyme A versus alpha-thrombin. *J Immunol* **156**, 2585–90 (1996).
- [195] Metkar, S. S. *et al.* Human and mouse granzyme A induce a proinflammatory cytokine response. *Immunity* **29**, 720–33 (2008).
- [196] Sower, L. E., Klimpel, G. R., Hanna, W. & Froelich, C. J. Extracellular activities of human granzymes. I. Granzyme A induces IL6 and IL8 production in fibroblast and epithelial cell lines. *Cell Immunol* **171**, 159–63 (1996).
- [197] Wensink, A. C. *et al.* Granzyme K synergistically potentiates LPS-induced cytokine responses in human monocytes. *Proc Natl Acad Sci U S A* **111**, 5974–9 (2014).
- [198] Spencer, C. T. *et al.* Granzyme A produced by $\gamma(9)\delta(2)$ T cells induces human macrophages to inhibit growth of an intracellular pathogen. *PLoS Pathog* **9**, e1003119 (2013).
- [199] Trapani, J. A. & Sutton, V. R. Granzyme B: pro-apoptotic, antiviral and antitumor functions. *Curr Opin Immunol* **15**, 533–43 (2003).
- [200] Odake, S. *et al.* Human and murine cytotoxic T lymphocyte serine proteases: subsite mapping with peptide thioester substrates and inhibition of enzyme activity and cytolysis by isocoumarins. *Biochemistry* **30**, 2217–27 (1991).
- [201] Atkinson, E. A. *et al.* Cytotoxic T lymphocyte-assisted suicide. Caspase 3 activation is primarily the result of the direct action of granzyme B. *J Biol Chem* **273**, 21261–6 (1998).

-
- [202] Sutton, V. R. *et al.* Initiation of apoptosis by granzyme B requires direct cleavage of bid, but not direct granzyme B-mediated caspase activation. *J Exp Med* **192**, 1403–14 (2000).
- [203] Sutton, V. R., Wowk, M. E., Cancilla, M. & Trapani, J. A. Caspase activation by granzyme B is indirect, and caspase autoprocessing requires the release of proapoptotic mitochondrial factors. *Immunity* **18**, 319–29 (2003).
- [204] Fellows, E., Gil-Parrado, S., Jenne, D. E. & Kurschus, F. C. Natural killer cell-derived human granzyme H induces an alternative, caspase-independent cell-death program. *Blood* **110**, 544–52 (2007).
- [205] Hou, Q. *et al.* Granzyme H induces apoptosis of target tumor cells characterized by DNA fragmentation and Bid-dependent mitochondrial damage. *Mol Immunol* **45**, 1044–55 (2008).
- [206] Ewen, C. L., Kane, K. P & Bleackley, R. C. Granzyme H induces cell death primarily via a Bcl-2-sensitive mitochondrial cell death pathway that does not require direct Bid activation. *Mol Immunol* **54**, 309–18 (2013).
- [207] Andrade, F., Fellows, E., Jenne, D. E., Rosen, A. & Young, C. S. H. Granzyme H destroys the function of critical adenoviral proteins required for viral DNA replication and granzyme B inhibition. *EMBO J* **26**, 2148–57 (2007).
- [208] Romero, V., Fellows, E., Jenne, D. E. & Andrade, F. Cleavage of La protein by granzyme H induces cytoplasmic translocation and interferes with La-mediated HCV-IRES translational activity. *Cell Death Differ* **16**, 340–8 (2009).
- [209] Zhao, T. *et al.* Granzyme K cleaves the nucleosome assembly protein SET to induce single-stranded DNA nicks of target cells. *Cell Death Differ* **14**, 489–99 (2007).
- [210] Hua, G., Wang, S., Zhong, C., Xue, P. & Fan, Z. Ignition of p53 bomb sensitizes tumor cells to granzyme K-mediated cytolysis. *J Immunol* **182**, 2152–9 (2009).
- [211] Cooper, D. M., Pechkovsky, D. V., Hackett, T. L., Knight, D. A. & Granville, D. J. Granzyme K activates protease-activated receptor-1. *PLoS One* **6**, e21484 (2011).
- [212] Bovenschen, N. *et al.* Granzyme K displays highly restricted substrate specificity that only partially overlaps with granzyme A. *J Biol Chem* **284**, 3504–12 (2009).
- [213] Bade, B. *et al.* Differential expression of the granzymes A, K and M and perforin in human peripheral blood lymphocytes. *Int Immunol* **17**, 1419–28 (2005).

- [214] Sayers, T. J. *et al.* The restricted expression of granzyme M in human lymphocytes. *J Immunol* **166**, 765–71 (2001).
- [215] de Koning, P. J. A. *et al.* The cytotoxic protease granzyme M is expressed by lymphocytes of both the innate and adaptive immune system. *Mol Immunol* **47**, 903–11 (2010).
- [216] de Poot, S. A. H. & Bovenschen, N. Granzyme M: behind enemy lines. *Cell Death Differ* **21**, 359–68 (2014).
- [217] Kelly, J. M. *et al.* Granzyme M mediates a novel form of perforin-dependent cell death. *J Biol Chem* **279**, 22236–42 (2004).
- [218] Hu, D. *et al.* Cleavage of survivin by Granzyme M triggers degradation of the survivin-X-linked inhibitor of apoptosis protein (XIAP) complex to free caspase activity leading to cytolysis of target tumor cells. *J Biol Chem* **285**, 18326–35 (2010).
- [219] de Poot, S. A. H. *et al.* Granzyme M targets topoisomerase II alpha to trigger cell cycle arrest and caspase-dependent apoptosis. *Cell Death Differ* **21**, 416–26 (2014).
- [220] Bovenschen, N. *et al.* NK cell protease granzyme M targets alpha-tubulin and disorganizes the microtubule network. *J Immunol* **180**, 8184–91 (2008).
- [221] Anthony, D. A. *et al.* A Role for Granzyme M in TLR4-Driven Inflammation and Endotoxemia. *J Immunol* **185**, 1794–1803 (2010).
- [222] Baschuk, N. *et al.* NK cell intrinsic regulation of MIP-1 α by granzyme M. *Cell Death Dis* **5**, e1115 (2014).
- [223] Krensky, A. M. & Clayberger, C. Biology and clinical relevance of granulysin. *Tissue Antigens* **73**, 193–8 (2009).
- [224] Stenger, S. *et al.* An antimicrobial activity of cytolytic T cells mediated by granulysin. *Science* **282**, 121–5 (1998).
- [225] Peña, S. V., Hanson, D. A., Carr, B. A., Goralski, T. J. & Krensky, A. M. Processing, subcellular localization, and function of 519 (granulysin), a human late T cell activation molecule with homology to small, lytic, granule proteins. *J Immunol* **158**, 2680–8 (1997).
- [226] Kaspar, A. A. *et al.* A distinct pathway of cell-mediated apoptosis initiated by granulysin. *J Immunol* **167**, 350–6 (2001).

-
- [227] Anderson, D. H. *et al.* Granulysin crystal structure and a structure-derived lytic mechanism. *J Mol Biol* **325**, 355–65 (2003).
- [228] Okada, S., Li, Q., Whitin, J. C., Clayberger, C. & Krensky, A. M. Intracellular mediators of granulysin-induced cell death. *J Immunol* **171**, 2556–62 (2003).
- [229] Lu, C.-C. *et al.* NK cells kill mycobacteria directly by releasing perforin and granulysin. *J Leukoc Biol* **96**, 1119–29 (2014).
- [230] Podack, E. R., Young, J. D. & Cohn, Z. A. Isolation and biochemical and functional characterization of perforin 1 from cytolytic T-cell granules. *Proc Natl Acad Sci U S A* **82**, 8629–33 (1985).
- [231] Bleackley, R. C. *et al.* The isolation and characterization of a family of serine protease genes expressed in activated cytotoxic T lymphocytes. *Immunol Rev* **103**, 5–19 (1988).
- [232] van den Broek, M. E. *et al.* Decreased tumor surveillance in perforin-deficient mice. *J Exp Med* **184**, 1781–90 (1996).
- [233] Stepp, S. E. *et al.* Perforin gene defects in familial hemophagocytic lymphohistiocytosis. *Science* **286**, 1957–9 (1999).
- [234] Pipkin, M. E. & Lieberman, J. Delivering the kiss of death: progress on understanding how perforin works. *Curr Opin Immunol* **19**, 301–8 (2007).
- [235] Podack, E. R., Konigsberg, P. J., Acha-Orbea, H., Pircher, H. & Hengartner, H. Cytolytic T-cell granules: biochemical properties and functional specificity. *Adv Exp Med Biol* **184**, 99–119 (1985).
- [236] Thiery, J. *et al.* Perforin pores in the endosomal membrane trigger the release of endocytosed granzyme B into the cytosol of target cells. *Nat Immunol* **12**, 770–7 (2011).
- [237] Treiner, E. Mucosal-associated invariant T cells in inflammatory bowel diseases: bystanders, defenders, or offenders? *Front Immunol* **6**, 27 (2015).
- [238] Oikonomou, K. G., Zachou, K. & Dalekos, G. N. Alpha-actinin: a multidisciplinary protein with important role in B-cell driven autoimmunity. *Autoimmun Rev* **10**, 389–96 (2011).
- [239] Honda, K. Actinin-4, a Novel Actin-bundling Protein Associated with Cell Motility and Cancer Invasion. *J Cell Biol* **140**, 1383–1393 (1998).

- [240] Tang, J., Taylor, D. W. & Taylor, K. A. The three-dimensional structure of alpha-actinin obtained by cryoelectron microscopy suggests a model for Ca(2+)-dependent actin binding. *J Mol Biol* **310**, 845–58 (2001).
- [241] Stanley, P. *et al.* Intermediate-affinity LFA-1 binds alpha-actinin-1 to control migration at the leading edge of the T cell. *EMBO J* **27**, 62–75 (2008).
- [242] Crosby, K. C. *et al.* Quantitative analysis of self-association and mobility of annexin A4 at the plasma membrane. *Biophys J* **104**, 1875–85 (2013).
- [243] Krendel, M. & Mooseker, M. S. Myosins: tails (and heads) of functional diversity. *Physiology (Bethesda)* **20**, 239–51 (2005).
- [244] Gálvez-Santisteban, M. *et al.* Synaptotagmin-like proteins control the formation of a single apical membrane domain in epithelial cells. *Nat Cell Biol* **14**, 838–49 (2012).
- [245] Gerke, V., Creutz, C. E. & Moss, S. E. Annexins: linking Ca²⁺ signalling to membrane dynamics. *Nat Rev Mol Cell Biol* **6**, 449–61 (2005).
- [246] D'Acquisto, F. *et al.* Impaired T cell activation and increased Th2 lineage commitment in Annexin-1-deficient T cells. *Eur J Immunol* **37**, 3131–42 (2007).
- [247] Gérard, S. *et al.* Human iNKT and MAIT cells exhibit a PLZF-dependent proapoptotic propensity that is counterbalanced by XIAP. *Blood* **121**, 614–23 (2013).
- [248] Santarlasci, V. *et al.* Rarity of human T helper 17 cells is due to retinoic acid orphan receptor-dependent mechanisms that limit their expansion. *Immunity* **36**, 201–14 (2012).
- [249] Santarlasci, V. *et al.* IL-4-induced gene 1 maintains high Tob1 expression that contributes to TCR unresponsiveness in human T helper 17 cells. *Eur J Immunol* **44**, 654–61 (2014).
- [250] Hsu, D. K., Chen, H.-Y. & Liu, F.-T. Galectin-3 regulates T-cell functions. *Immunol Rev* **230**, 114–27 (2009).
- [251] Stillman, B. N. *et al.* Galectin-3 and galectin-1 bind distinct cell surface glycoprotein receptors to induce T cell death. *J Immunol* **176**, 778–89 (2006).
- [252] He, J. & Baum, L. G. Presentation of galectin-1 by extracellular matrix triggers T cell death. *J Biol Chem* **279**, 4705–12 (2004).

-
- [253] Hayashi, K., Jutabha, P., Endou, H., Sagara, H. & Anzai, N. LAT1 is a critical transporter of essential amino acids for immune reactions in activated human T cells. *J Immunol* **191**, 4080–5 (2013).
- [254] Gaardbo, J. C. *et al.* Increased Tryptophan Catabolism is Associated with Increased Frequency of CD161+Tc17/MAIT Cells, and Lower CD4+ T cell Count in HIV-1 infected Patients on cART after Two Years of Follow-up. *J Acquir Immune Defic Syndr* (2015).
- [255] Wright, N. T., Cannon, B. R., Zimmer, D. B. & Weber, D. J. S100A1: Structure, Function, and Therapeutic Potential. *Curr Chem Biol* **3**, 138–145 (2009).
- [256] Gross, S. R., Sin, C. G. T., Barraclough, R. & Rudland, P. S. Joining S100 proteins and migration: for better or for worse, in sickness and in health. *Cell Mol Life Sci* **71**, 1551–79 (2014).
- [257] Yokohama, A. *et al.* A novel mouse model for the aggressive variant of NK cell and T cell large granular lymphocyte leukemia. *Leuk Res* **34**, 203–9 (2010).
- [258] Robertson, M. J. *et al.* Characterization of a cell line, NKL, derived from an aggressive human natural killer cell leukemia. *Exp Hematol* **24**, 406–15 (1996).
- [259] McAlister, G. C. *et al.* MultiNotch MS3 enables accurate, sensitive, and multiplexed detection of differential expression across cancer cell line proteomes. *Anal Chem* **86**, 7150–8 (2014).
- [260] Kawachi, I., Maldonado, J., Strader, C. & Gilfillan, S. MR1-Restricted V α 19i Mucosal-Associated Invariant T Cells Are Innate T Cells in the Gut Lamina Propria That Provide a Rapid and Diverse Cytokine Response. *J Immunol* **176**, 1618–1627 (2006).
- [261] Janoir, C. *et al.* Adaptive strategies and pathogenesis of *Clostridium difficile* from in vivo transcriptomics. *Infect Immun* **81**, 3757–69 (2013).
- [262] Instructions to Authors. *Eur J Biochem* **267**, 276–276 (2000).

Acknowledgments

Mein ausdrücklicher und besonderer Dank gilt zuallererst meinem Mentor Prof. Dr. Lothar Jän-sch. Einerseits für die Möglichkeit, unter seiner Aufsicht meine Promotion am HelmholtzZen-trum für Infektionsforschung durchführen zu dürfen. Andererseits, und dafür im speziellen, für die hervorragende fachliche Betreuung und Unterstützung während der vergangenen vier Jahre, die vielen Mühen und das erbrachte Vertrauen. Des Weiteren danke ich Prof. Dr. Dunja Bruder und Prof. Dr. Stephan Dübel für die freundliche Übernahme des Korrefendariats. Ich möchte mich bei Dr. Sabine Kirchhoff und dem Team der Graduiertenschule des HZI bedanken, für die Unterstützung bei verwaltungstechnischen Angelegenheiten. Meinen Ko-operationspartnern Dr. Henk Garritsen und Prof. Dr. Johan Sandberg möchte ich für die gute Zusammenarbeit danken, und insbesondere Dr. Lothar Gröbe für die Unterstützung bei den durchflusszytometrischen Sortiervverfahren. Der gesamten Arbeitsgruppe Zelluläre Proteom-forschung gilt mein besonderer Dank für die vielfältige Unterstützung, und die unglaubliche Arbeitsatmosphäre. Ich möchte mich ausdrücklich bei Amanda Mühlmann für die Unter-stützung bei verwaltungstechnischen und organisatorischen Angelegenheiten bedanken, bei Dr. Josef Wissing für die Unterstützung bei den massenspektrometischen Arbeiten, sowie bei Reiner Munder, Undine Felgenträger und Kirsten Minkhart für die exzellente technische Assistenz. Dr. Marco van Ham und Dr. Maxi Heyner danke ich für die vielfältige fachliche Unterstützung während unterschiedlicher Phasen meiner Promotion, sowie Mario Schmidt und Maxi für die tolle gemeinsame Zeit im gleichen Büro. Ein besonderer Dank gilt hier noch dem Rest von CPRO, den ich nicht erwähnt habe, sowie den vielen lieben Menschen aus dem A-Gebäude Zuletzt möchte ich denen Menschen danken, die mir am nächsten stehen. Meine Familie und Freunde haben mich während der Promotion stets bedingungslos unterstützt, dafür kann ich nicht genug dankbar sein. Dhana danke ich für jede Sekunde.